FILE COVERS 1907 - 16 Oct 2004 VOL 141 ISS 17
FILE LAST UPDATED: 15 Oct 2004 (20041015/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=>
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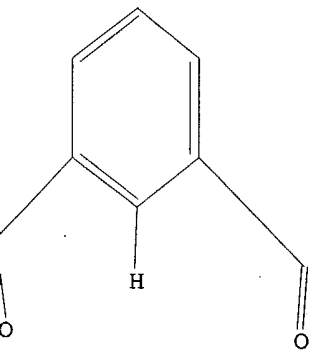
L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1 full
REGISTRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

FULL SEARCH INITIATED 13:48:24 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 497633 TO ITERATE

80.4% PROCESSED 400000 ITERATIONS 60742 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.03

FULL FILE PROJECTIONS: ONLINE **INCOMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 497633 TO 497633
PROJECTED ANSWERS: 74744 TO 76392

L2 60742 SEA SSS FUL L1

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L3       23323 L2

=> s l3 and py<2001
      20629913 PY<2001
L4       17182 L3 AND PY<2001

=> s l4 and treat?
       3094869 TREAT?
L5        2693 L4 AND TREAT?

=> s l5 and (breast carcinoma or rheumatoid arthritis or osteoarthritis or heart failure)
         56517 BREAST
        115548 CARCINOMA
          5773 BREAST CARCINOMA
                 (BREAST(W)CARCINOMA)
         23701 RHEUMATOID
         34066 ARTHRITIS
         20506 RHEUMATOID ARTHRITIS
                 (RHEUMATOID(W)ARTHRITIS)
          5833 OSTEOARTHRITIS
        294581 HEART
        160480 FAILURE
         16179 HEART FAILURE
                 (HEART(W)FAILURE)
L6          27 L5 AND (BREAST CARCINOMA OR RHEUMATOID ARTHRITIS OR OSTEOARTHRIT
               IS OR HEART FAILURE)

=> d 1-27, ibib abs hitstr

L6   ANSWER 1 OF 27  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2000:881130  CAPLUS
DOCUMENT NUMBER:          134:42124
TITLE:                    Preparation of diaminothiazoles for inhibiting protein
                          kinases
INVENTOR(S):              Chu, Shao Song; Alegria, Larry Andrew; Bender, Steven
                          Lee; Benedict, Suzanne Pritchett; Borchardt, Allen J.;
                          Kania, Robert Steve; Nambu, Mitchell David;
                          Tempczyk-Russell, Anna Maria; Sarshar, Sepehr
PATENT ASSIGNEE(S):       Agouron Pharmaceuticals, Inc., USA
SOURCE:                   PCT Int. Appl., 397 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

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     WO 2000075120         A1    20001214    WO 2000-US15188          20000602 <--
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             CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID,
             IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV,
             MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG,
             SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
             CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     EP 1181283            A1    20020227    EP 2000-942660           20000602
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
     BR 2000011585         A     20020319    BR 2000-11585            20000602
     JP 2003501420         T2    20030114    JP 2001-501601           20000602
     EE 200100659          A     20030217    EE 2001-659              20000602
     US 2002025976         A1    20020228    US 2001-783584           20010215
     US 6620828            B2    20030916
     ZA 2001008291         A     20021009    ZA 2001-8291             20011009
     NO 2001005045         A     20020204    NO 2001-5045             20011017
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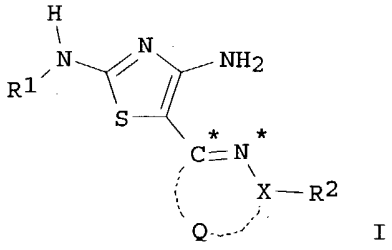
BG 106276 A 20021031 BG 2002-106276 20020103
PRIORITY APPLN. INFO.: US 1999-137810P P 19990604
US 2000-587530 B1 20000602
WO 2000-US15188 W 20000602
OTHER SOURCE(S): MARPAT 134:42124
GI



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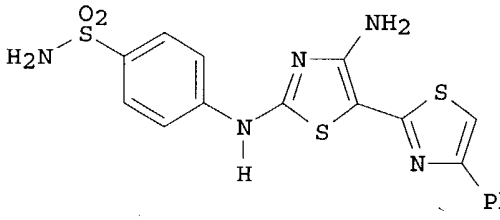


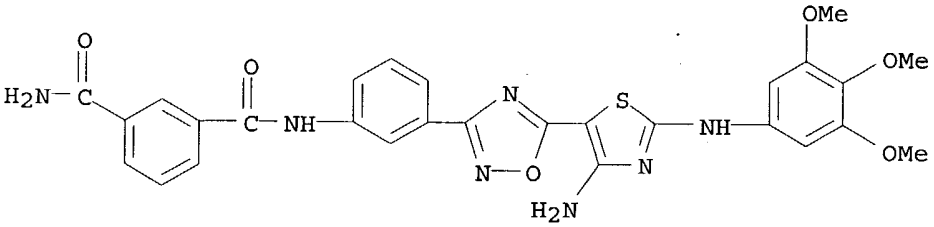
II

AB The title compds. [I; R1 = H, (un)substituted alkyl, cycloalkyl, etc.; R2 = OH, halo, CN, etc.; X = C, N; Q = a divalent radical having 2 or 3 atoms selected from C, N, O, S, CR5, NR5 (wherein R5 = OH, halo, CN, etc.) which together with C* and N* form a 5-6 membered (non)aromatic ring] which modulate and/or inhibit the activity of certain protein kinases (biol. data were given), and are useful in **treating** cancer as well as other disease states associated with unwanted angiogenesis and/or cellular proliferation, such as diabetic retinopathy, neovascular glaucoma, **rheumatoid arthritis**, and psoriasis, were prepared and formulated. E.g., a multi-step synthesis of diaminothiazole II was given. The compds. I and pharmaceutical compns. containing them are capable of mediating tyrosine kinase signal transduction in order to modulate and/or inhibit unwanted cell proliferation.

IT **312763-38-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of diaminothiazoles for inhibiting protein kinases)

RN 312763-38-5 CAPLUS

CN 1,3-Benzenedicarboxamide, N-[3-[5-[4-amino-2-[(3,4,5-trimethoxyphenyl)amino]-5-thiazolyl]-1,2,4-oxadiazol-3-yl]phenyl]- (9CI) (CA INDEX NAME)

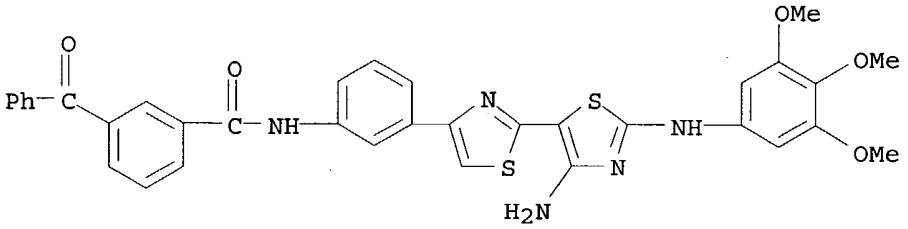


IT **312769-34-9 312770-65-3 312770-77-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of diaminothiazoles for inhibiting protein kinases)

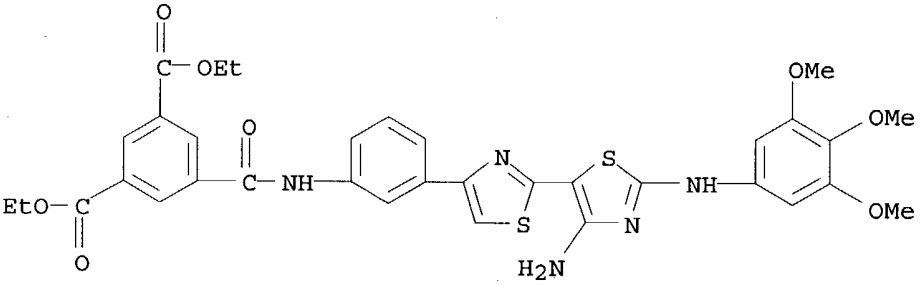
RN 312769-34-9 CAPLUS

CN Benzamide, N-[3-[4'-amino-2'-[(3,4,5-trimethoxyphenyl)amino][2,5'-bithiazol]-4-yl]phenyl]-3-benzoyl- (9CI) (CA INDEX NAME)



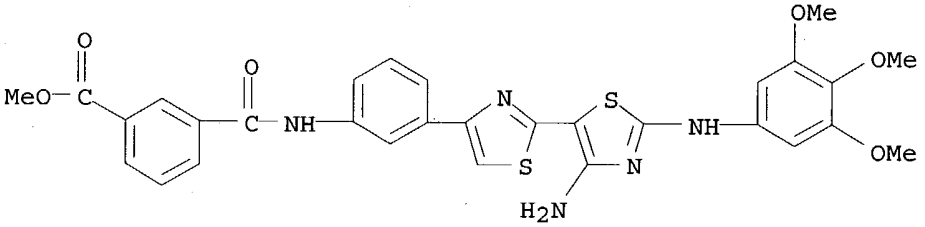
RN 312770-65-3 CAPLUS

CN 1,3-Benzenedicarboxylic acid, 5-[[[3-[4'-amino-2'-[(3,4,5-trimethoxyphenyl)amino][2,5'-bithiazol]-4-yl]phenyl]amino]carbonyl]-, diethyl ester (9CI) (CA INDEX NAME)



RN 312770-77-7 CAPLUS

CN Benzoic acid, 3-[[[3-[4'-amino-2'-[(3,4,5-trimethoxyphenyl)amino][2,5'-bithiazol]-4-yl]phenyl]amino]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:824101 CAPLUS

DOCUMENT NUMBER: 134:5154

TITLE: Preparation of cyclic amine derivatives as remedies or preventives for diseases in association with chemokines or chemokine receptors

INVENTOR(S): Shiota, Tatsuki; Miyagi, Fuminori; Kamimura, Takashi; Ohta, Tomohiro; Takano, Yasuhiro; Horiuchi, Hideki

PATENT ASSIGNEE(S): Teijin Limited, Japan

SOURCE: PCT Int. Appl., 405 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000069432	A1	20001123	WO 2000-JP3203	20000518 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1179341	A1	20020213	EP 2000-927808	20000518
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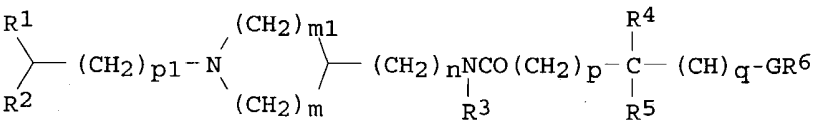
NZ 515374	A	20040924	NZ 2000-515374	20000518
NO 2001005599	A	20011116	NO 2001-5599	20011116
PRIORITY APPLN. INFO.:			JP 1999-175856 A	19990518
			JP 1999-251464 A	19990906
			WO 2000-JP3203 W	20000518

OTHER SOURCE(S): MARPAT 134:5154

GI



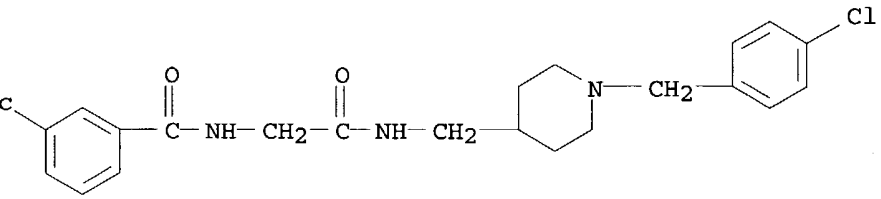
I

AB Remedies or preventives for diseases in association with chemokines such as MIP-1α and/or MCP-1 or chemokine receptors such as CCR1 or CCR2 contain as the active ingredient N-acyl-amino acid N-cyclic amino or N-cyclic aminoalkyl-amide derivs. represented by general formula [I; (un)substituted Ph, C3-8 cycloalkyl, aromatic heterocyclyl containing 1-3 heteroatoms selected from O, S, and/or N; R2 = H, (un)substituted C1-6 alkyl, C2-7 alkoxycarbonyl, HO, (un)substituted Ph; p1, m1 = 0-2; m = 2-4; n = 0,1; R3 = H, (un)substituted C1-6 alkyl; R4, R5 = H, OH, (un)substituted Ph or C1-6 alkyl; or R4 and R5 are combined together to form a 3- to 5-membered hydrocarbyl; p, q = 0,1; G = CO, SO2, CO2, NR7CO, CONR7, NR7SO2, or SO2NR7, NHCONH, NHCSNH, NH CO2, O2CNH; R7 = H, C1-6 alkyl; or R7 and R5 are combined together to form C2-5 alkylene; R6 = (un)substituted Ph, C3-8 cycloalkyl, C3-6 cycloalkenyl, CH2Ph, or aromatic heterocyclyl containing 1-3 heteroatoms selected from O, S, and/or N, wherein Ph, CH2Ph, or aromatic heterocyclyl group is optionally fused with (un)substituted benzene or aromatic heterocyclyl containing 1-3 heteroatoms selected from O, S, and/or N], pharmaceutically acceptable acid-adducts thereof, or pharmaceutically acceptable C1-6 alkyl-adducts thereof. The above diseases include destruction of bone or cartilage (e.g. arthritis, **rheumatoid arthritis**, **osteoarthritis**, osteoporosis, injury, and tumor), nephritis, kidney diseases, glomerulus or interstitial nephritis, nephrotic syndrome, demyelinating disease, or multiple sclerosis. Thus, N-3-ethoxybenzyl-D-methionine-N-[1-(4-chlorobenzyl)-4-piperazinylmethyl]amide in vitro inhibited the binding of human MIP-1α to THP-1 cells by >80% at 2 μM.

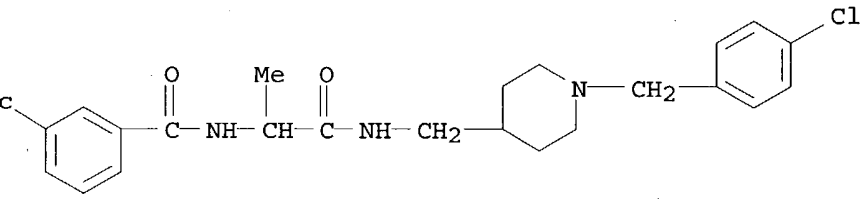
IT **226231-26-1P 226232-13-9P 226232-44-6P**
226232-66-2P 226232-70-8P 226233-64-3P
226233-91-6P 226241-34-5P 226241-35-6P
226241-39-0P 226241-41-4P 308360-90-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cyclic amine derivs. as remedies or preventives for diseases in association with chemokines or chemokine receptors)

RN 226231-26-1 CAPLUS

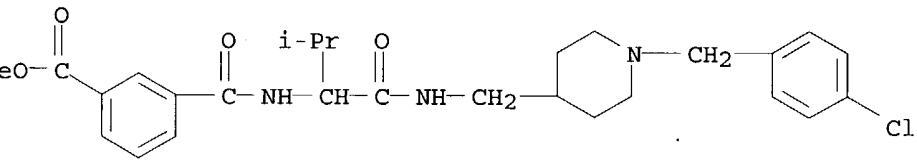
CN Benzamide, 3-acetyl-N-[2-[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)



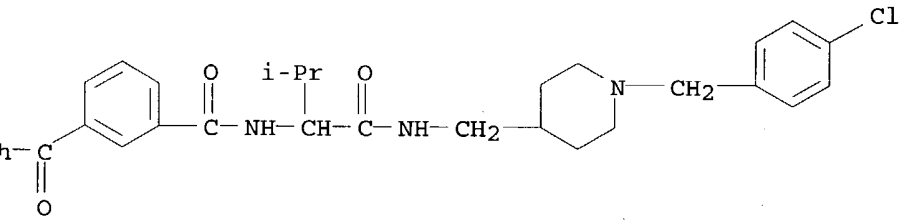
N 226232-13-9 CAPLUS
N Benzamide, 3-acetyl-N-[2-[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]-1-methyl-2-oxoethyl]- (9CI) (CA INDEX NAME)



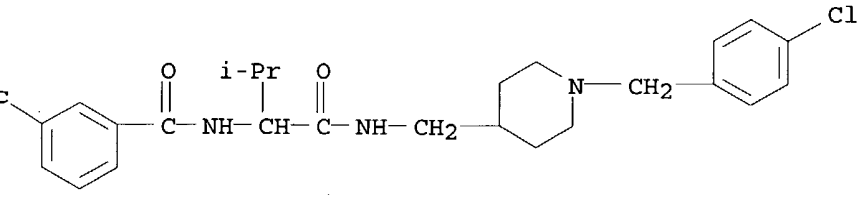
N 226232-44-6 CAPLUS
N Benzoic acid, 3-[[[1-[[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]carbonyl]-2-methylpropyl]amino]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



N 226232-66-2 CAPLUS
N Benzamide, 3-benzoyl-N-[1-[[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]carbonyl]-2-methylpropyl]- (9CI) (CA INDEX NAME)

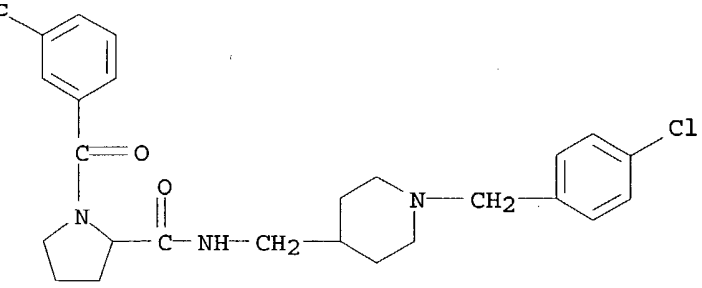


N 226232-70-8 CAPLUS
N Benzamide, 3-acetyl-N-[1-[[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]carbonyl]-2-methylpropyl]- (9CI) (CA INDEX NAME)

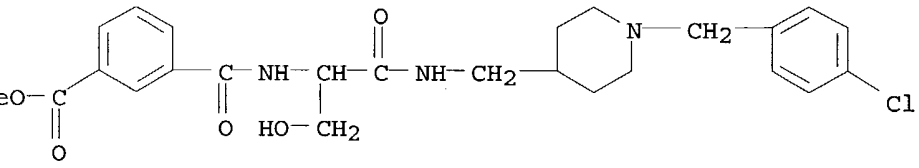


N 226233-64-3 CAPLUS

N 2-Pyrrolidinecarboxamide, 1-(3-acetylbenzoyl)-N-[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)

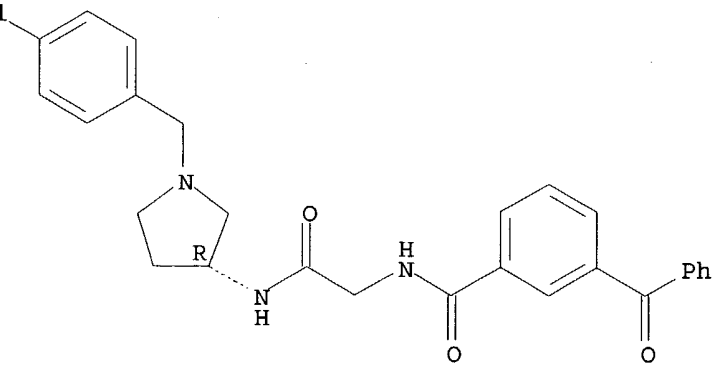


N 226233-91-6 CAPLUS
N Benzoic acid, 3-[[[2-[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]-1-(hydroxymethyl)-2-oxoethyl]amino]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



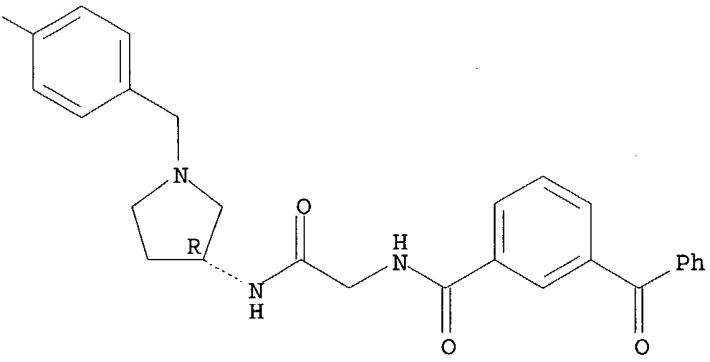
N 226241-34-5 CAPLUS
N Benzamide, 3-benzoyl-N-[2-[[(3R)-1-[(4-chlorophenyl)methyl]-3-pyrrolidinyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

bsolute stereochemistry.



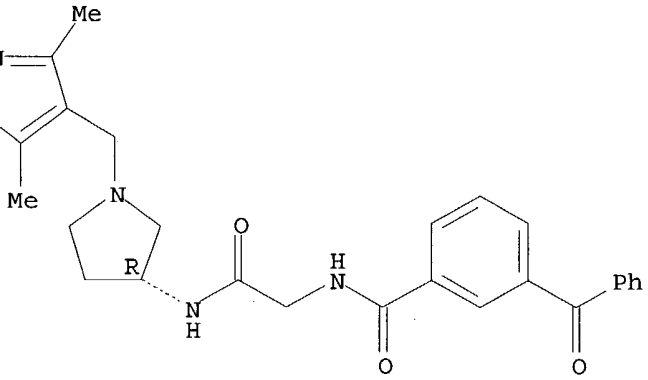
N 226241-35-6 CAPLUS
N Benzamide, 3-benzoyl-N-[2-[[(3R)-1-[(4-methylphenyl)methyl]-3-pyrrolidinyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

bsolute stereochemistry.

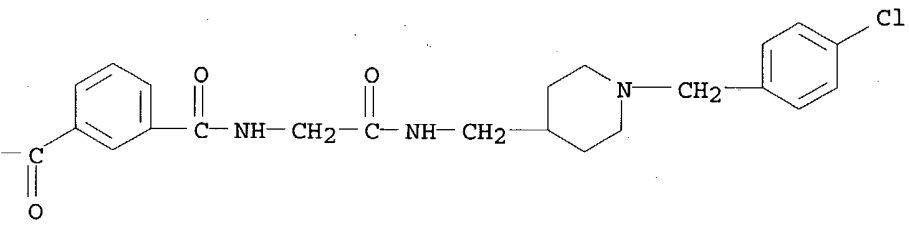


226241-39-0 CAPLUS
Benzamide, 3-benzoyl-N-[2-[[(3R)-1-[(3,5-dimethyl-4-isoxazolyl)methyl]-3-pyrrolidinyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

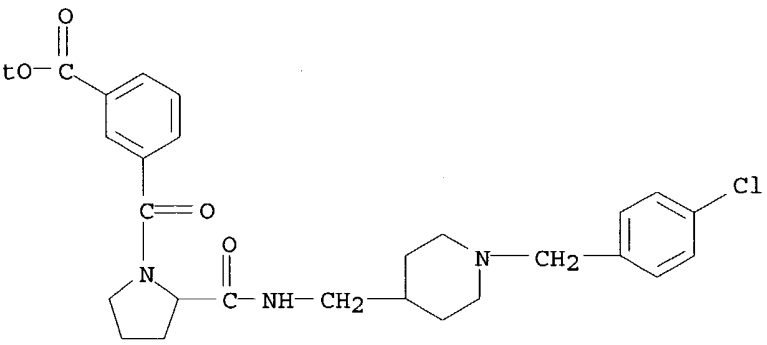
solute stereochemistry.



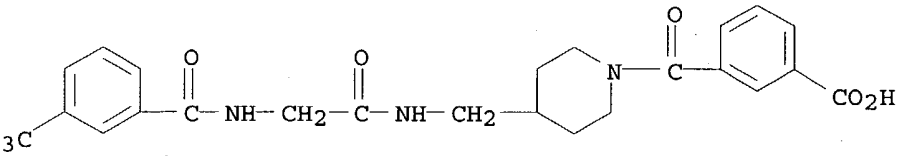
226241-41-4 CAPLUS
Benzamide, 3-benzoyl-N-[2-[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)



308360-90-9 CAPLUS
Benzoic acid, 3-[[2-[[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]carbonyl]-1-pyrrolidinyl]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)



T **308363-03-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of cyclic amine derivs. as remedies or preventives for diseases in association with chemokines or chemokine receptors)
N 308363-03-3 CAPLUS
N Benzoic acid, 3-[[4-[[[[[3-(trifluoromethyl)benzoyl]amino]acetyl]amino]methyl]-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)



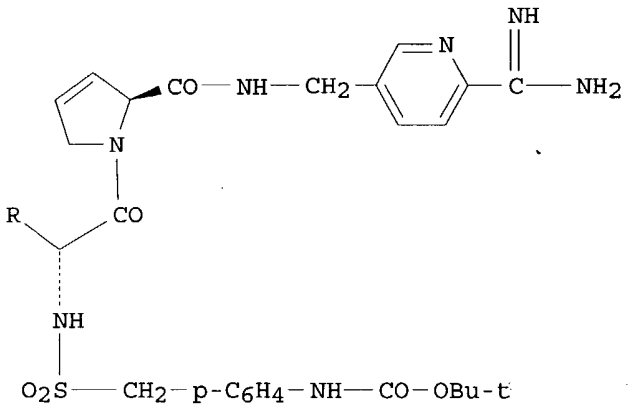
EFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

6 ANSWER 3 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
CCESSION NUMBER: 2000:742117 CAPLUS
OCUMENT NUMBER: 133:296665
ITLE: Preparation of amidine- or guanidine-containing peptidomimetics for use as inhibitors of complement proteases
NVENTOR(S): Hillen, Heinz; Schmidt, Martin; Mack, Helmut; Seitz, Werner; Haupt, Andreas; Zechel, Johann-Christian; Kling, Andreas
ATENT ASSIGNEE(S): BASF A.-G., Germany
OURCE: PCT Int. Appl., 212 pp.
CODEN: PIXXD2
OCUMENT TYPE: Patent
ANGUAGE: German
AMILY ACC. NUM. COUNT: 4
ATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000061608	A2	20001019	WO 2000-EP2710	20000328 <--
WO 2000061608	A3	20010111		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1169338	A2	20020109	EP 2000-920597	20000328
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200102913	T2	20020121	TR 2001-200102913	20000328
BR 2000009678	A	20020122	BR 2000-9678	20000328

JP 2002542164	T2	20021210	JP 2000-611550		20000328
US 6683055	B1	20040127	US 2000-539811		20000330
ZA 2001007978	A	20030107	ZA 2001-7978		20010928
BG 105978	A	20020731	BG 2001-105978		20011004
NO 2001004876	A	20011204	NO 2001-4876		20011008
PRIORITY APPLN. INFO.:			DE 1999-19915930	A	19990409
			WO 2000-EP2710	W	20000328

OTHER SOURCE(S): MARPAT 133:296665
GI



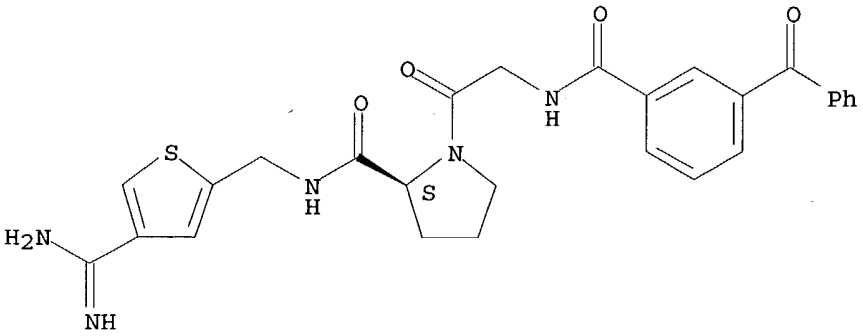
I

AB The invention relates to synthesis of title compds., e.g. [I; R = cyclohexyl(II) or R = cyclohexylmethyl(III)], for use as inhibitors of the complement proteases C1s and C1r in **treatment** of disease. Compound III was synthesized in seven steps, beginning with (D)-cyclohexylalanine Me ester hydrochloride and 4-nitrobenzylsulfonyl chloride, and including reaction with 3,4-dehydroprolyl-(3-(6-cyano)picolyl)-amide and conversion of the cyano group to the amidine. In in vivo expts. II had IC50's for C1s and C1r resp. of 0.6 and 0.9 μmol/l.

IT **301189-33-3P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amidine- or guanidine-containing peptidomimetics for use as inhibitors of complement proteases)

RN 301189-33-3 CAPLUS
CN L-Prolinamide, N-(3-benzoylbenzoyl)glycyl-N-[[4-(aminoiminomethyl)-2-thienyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 4 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:475535 CAPLUS
DOCUMENT NUMBER: 133:99557

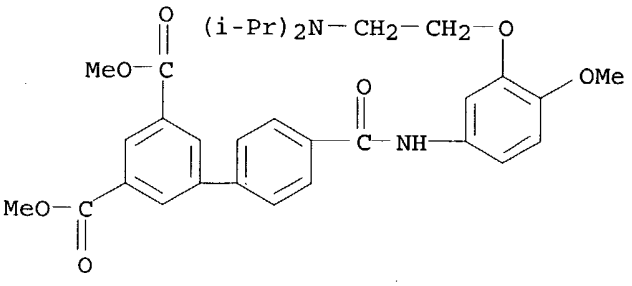
TITLE: Substituted benzanilides, their preparation, and their use as CCR5 receptor modulators
INVENTOR(S): Bondinell, William E.; Ku, Thomas W.; Wang, Ning
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000040239	A1	20000713	WO 1999-US30888	19991228 <--
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1140072	A1	20011010	EP 1999-967619	19991228
EP 1140072	B1	20040414		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002534383	T2	20021015	JP 2000-591996	19991228
AT 264100	E	20040415	AT 1999-967619	19991228

PRIORITY APPLN. INFO.:
US 1998-114239P P 19981230
US 1999-128010P P 19990406
WO 1999-US30888 W 19991228

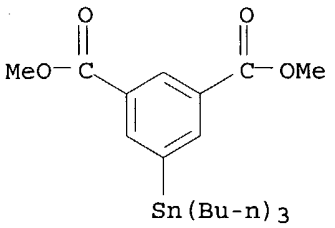
AB Substituted benzanilides are provided which are modulators, agonists or antagonists, of the CCR5 receptor. In addition, the invention relates to the **treatment** and prevention of disease states mediated by CCR5, including, but not limited to, asthma and atopic disorders (for example, atopic dermatitis and allergies), **rheumatoid arthritis**, sarcoidosis and other fibrotic diseases, atherosclerosis, psoriasis, autoimmune diseases such as multiple sclerosis, and inflammatory bowel disease, all in mammals, by the use of substituted benzanilides which are CCR5 receptor antagonists. Furthermore, since CD8+ T cells have been implicated in COPD, CCR5 may play a role in their recruitment and therefore antagonists to CCR5 could provide potential therapeutic in the **treatment** of COPD. Also, since CCR5 is a co-receptor for the entry of HIV into cells, selective receptor modulators may be useful in the **treatment** of HIV infection.

IT **282727-17-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(benzanilide derivative preparation and use as CCR5 receptor modulator)
RN 282727-17-7 CAPLUS
CN [1,1'-Biphenyl]-3,5-dicarboxylic acid, 4'-[[[3-[2-[bis(1-methylethyl)amino]ethoxy]-4-methoxyphenyl]amino]carbonyl]-, dimethyl ester (9CI) (CA INDEX NAME)



IT **210094-16-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; benzanilide derivative preparation and use as CCR5 receptor modulator)
RN 210094-16-9 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-(tributylstannyl)-, dimethyl ester (9CI)

(CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:335229 CAPLUS
DOCUMENT NUMBER: 132:343358
TITLE: Cystine derivatives as therapeutic agents for matrix metalloprotease-related diseases
INVENTOR(S): Grams, Frank; Krell, Hans-Willi; Leinert, Herbert; Zimmermann, Gerd
PATENT ASSIGNEE(S): Roche Diagnostics G.m.b.H., Germany
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000027378	A2	20000518	WO 1999-EP8460	19991105 <--
WO 2000027378	A3	20010920		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 9915127	A	20010731	BR 1999-15127	19991105
EP 1143960	A2	20011017	EP 1999-971709	19991105
EP 1143960	A3	20011205		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200101222	T2	20011221	TR 2001-200101222	19991105
JP 2002529404	T2	20020910	JP 2000-580607	19991105
ZA 2001003605	A	20011211	ZA 2001-3605	20010504

PRIORITY APPLN. INFO.: EP 1998-121073 A 19981106
WO 1999-EP8460 W 19991105

OTHER SOURCE(S): MARPAT 132:343358

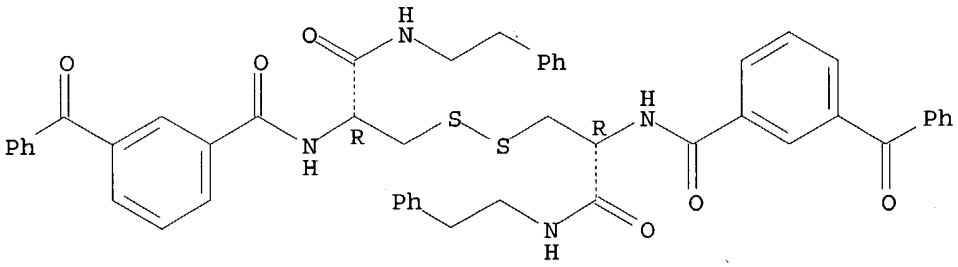
AB Pharmaceutical compns. are disclosed which contain nonpeptidic cystine derivs. R1ANHCH[CH2SSCH2CH(R3ANH)(C(O)NHR4)]C(O)NHR2 [R1, R3 = H, (non)aromatic carbocyclic or heterocyclic ring, (un)branched (un)saturated C1-15 alkyl which can be interrupted by hetero atom and which can be substituted by (non)aromatic carbocyclic or heterocyclic ring; R2, R4 = H, (un)branched (un)saturated C1-15 alkyl which can be interrupted by hetero atom and which can be substituted by (non)aromatic carbocyclic or heterocyclic ring; A = valency bond, CO, SO2, NHCO, NHCS or OC(O)], their pharmacol. acceptable salts and optically active forms thereof and pharmaceutically acceptable carriers, for the **treatment** of diseases selected from tumor growth and metastasis; inflammatory diseases, e.g. osteo- and **rheumatoid arthritis**; osteoporosis; multiple sclerosis; periodontitis; restenosis; diseases caused by bacteria, e.g. meningitis; sun-induced skin aging; and Alzheimer's disease. New compds. are also

disclosed.

IT **269067-09-6P 269067-10-9P 269067-11-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cystine derivative for **treatment** of matrix metalloprotease-related disease)

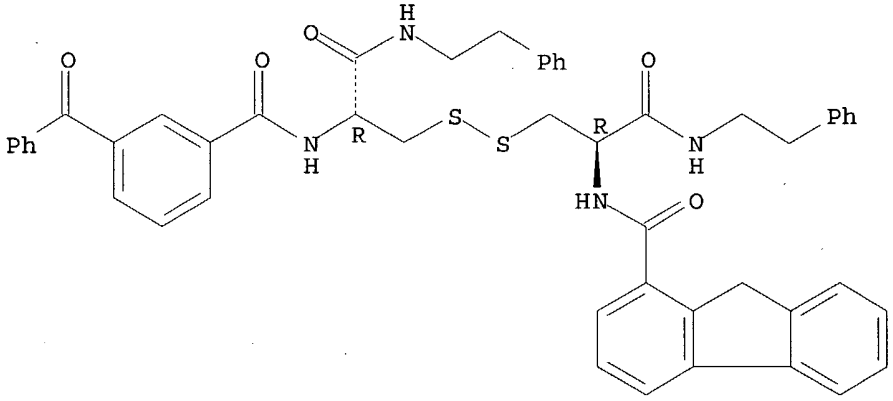
RN 269067-09-6 CAPLUS
CN Benzamide, N,N'-[dithiobis[(1R)-1-[[(2-phenylethyl)amino]carbonyl]-2,1-ethanediyl]]bis[3-benzoyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



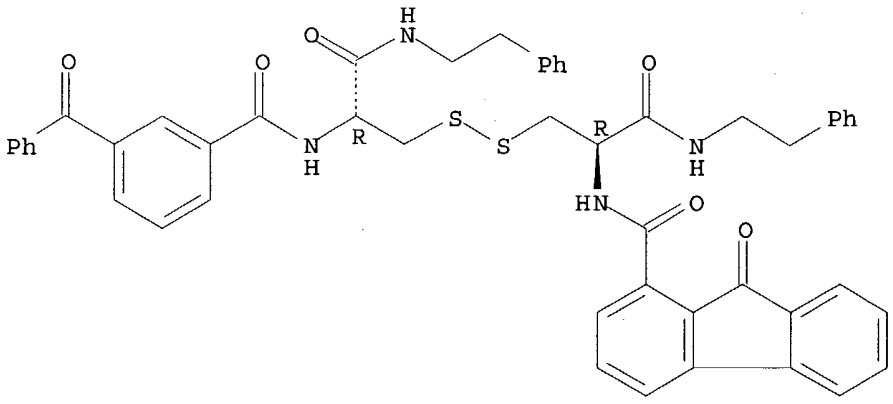
RN 269067-10-9 CAPLUS
CN 9H-Fluorene-1-carboxamide, N-[(1R)-1-[[[(2R)-2-[(3-benzoylbenzoyl)amino]-3-oxo-3-[(2-phenylethyl)amino]propyl]dithio]methyl]-2-oxo-2-[(2-phenylethyl)amino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 269067-11-0 CAPLUS
CN 9H-Fluorene-1-carboxamide, N-[(1R)-1-[[[(2R)-2-[(3-benzoylbenzoyl)amino]-3-oxo-3-[(2-phenylethyl)amino]propyl]dithio]methyl]-2-oxo-2-[(2-phenylethyl)amino]ethyl]-9-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 6 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:260225 CAPLUS
DOCUMENT NUMBER: 132:294010
TITLE: Preparation of diaminopropionic acid derivatives as intracellular adhesion molecule-1 (ICAM-1) binding inhibitors
INVENTOR(S): Fotouhi, Nader; Gillespie, Paul; Guthrie, Robert William; Pietranico-Cole, Sherrie Lynn; Yun, Weiya
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 259 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000021920	A1	20000420	WO 1999-EP7620	19991012 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6331640	B1	20011218	US 1999-407534	19990929
CA 2344058	AA	20000420	CA 1999-2344058	19991012 <--
BR 9914602	A	20010703	BR 1999-14602	19991012
EP 1121342	A1	20010808	EP 1999-953772	19991012
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200101038	T2	20010921	TR 2001-200101038	19991012
JP 2002527416	T2	20020827	JP 2000-575829	19991012
AU 766468	B2	20031016	AU 2000-10349	19991012
ZA 2001002608	A	20020930	ZA 2001-2608	20010329
US 2002052512	A1	20020502	US 2001-879700	20010612
US 2004006236	A1	20040108	US 2003-349289	20030122
US 6803384	B2	20041012		

PRIORITY APPLN. INFO.:	US 1998-104120P	P	19981013
	US 1999-407534	A3	19990929
	WO 1999-EP7620	W	19991012
	US 2001-879700	B3	20010612

OTHER SOURCE(S): MARPAT 132:294010
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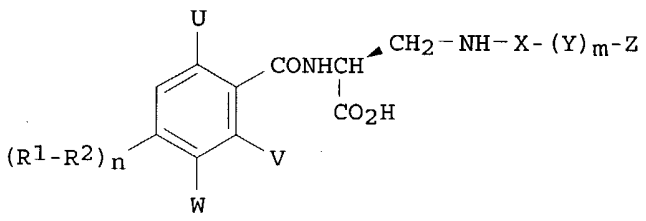


I

AB Diaminopropionic acid derivs. I [R1 = substituted 1-naphthyl, 4-indolyl, 4-benzimidazolyl, 4-benzodiazolyl, 4-benzotriazolyl, or phenyl; R2 = CHR3NHCO (R3 = H, carboxy, alkyl), CH2CH2CO, 1,2-cyclopropanediylcarbonyl, OCH2CO, CH:CHCHR3, CH2CH2CH(OH), CONHCHR3, or CH2NH-5,1-tetrazolediyl; U, V, W = H, halo, alkyl provided that U and V are not both hydrogen; X = CO, phenylalkylene, sulfonyl; Y = alkylene which may be substituted by amino or cycloalkyl, alkenylene, alkylenethio; Z = H, alkylthio, CO2H, CONH2, 1-adamantyl, diphenylmethyl, 3-[[(5-chloro-2-pyridinyl)amino]carbonyl]-2-

pyrazinyl, hydroxy, phenylmethoxy, 2-chloro-4-[[[(3-hydroxyphenyl)methyl]amino]carbonyl]phenyl, [(2,6-dichlorophenyl)methoxy], Ph, (un)substituted cycloalkyl or aryl or fused ring system which may contain 0-3 heteroatoms; m, n = 0, 1] or their pharmaceutically acceptable salts or esters were prepared and are useful for **treating rheumatoid arthritis**, psoriasis, multiple sclerosis, Crohn's disease, ulcerative colitis, atherosclerosis, restenosis, pancreatitis, transplant rejection, delayed graft function and diseases of ischemia reperfusion injury, including acute myocardial infarction and stroke. Thus, N-[2-chloro-4-[[[(3-hydroxyphenyl)methyl]amino]carbonyl]benzoyl]-3-(3-methoxybenzoylamino)-L-alanine was prepared by the solid-phase method and showed IC50 = 1.2 nM in the LFA-1 (lymphocyte function-associated antigen-1)/ICAM-1 protein-protein assay.

IT **264273-81-6P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

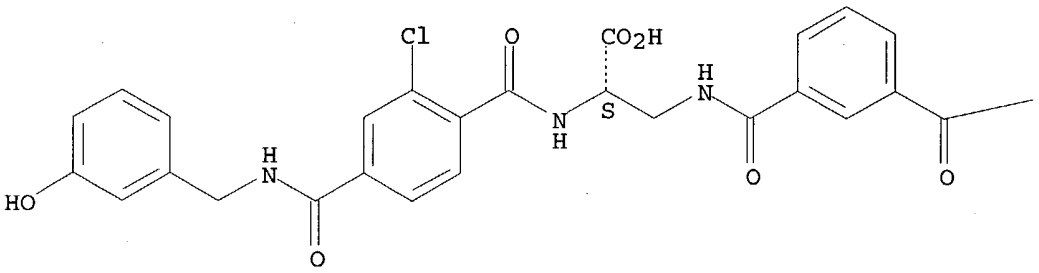
(preparation of diaminopropionic acid derivs. as intracellular adhesion mol.-1 (ICAM-1) binding inhibitors)

RN 264273-81-6 CAPLUS

CN Benzoic acid, 3-[[[(2S)-2-carboxy-2-[[2-chloro-4-[[[(3-hydroxyphenyl)methyl]amino]carbonyl]benzoyl]amino]ethyl]amino]carbonyl]-, 1-methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

—OMe

IT **264274-87-5P 264275-30-1P**

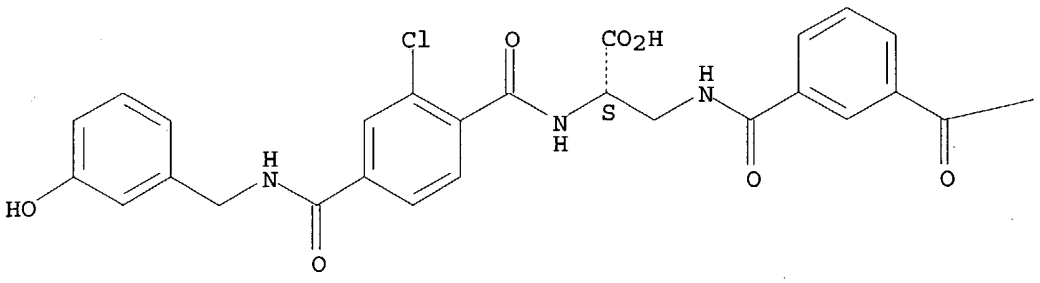
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of diaminopropionic acid derivs. as intracellular adhesion mol.-1 (ICAM-1) binding inhibitors)

RN 264274-87-5 CAPLUS

CN L-Alanine, 3-[[3-(aminocarbonyl)benzoyl]amino]-N-[2-chloro-4-[[[(3-hydroxyphenyl)methyl]amino]carbonyl]benzoyl]- (9CI) (CA INDEX NAME)

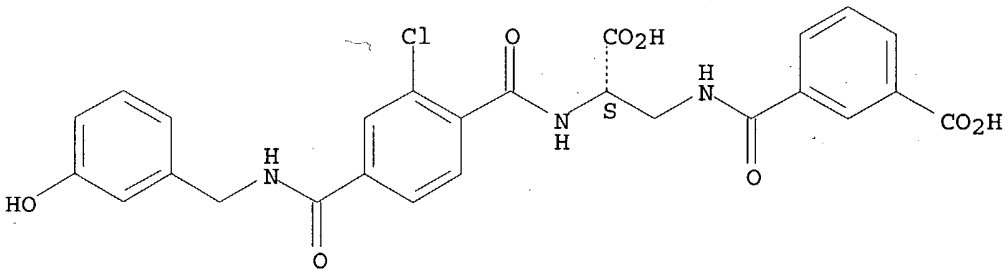
Absolute stereochemistry.



—NH_2

RN 264275-30-1 CAPLUS
CN Benzoic acid, 3-[[[(2S)-2-carboxy-2-[[2-chloro-4-[[[(3-hydroxyphenyl)methyl]amino]carbonyl]benzoyl]amino]ethyl]amino]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

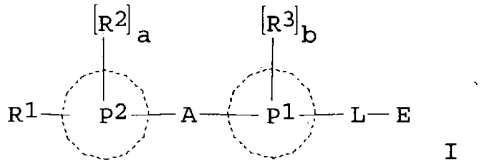
L6 ANSWER 7 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:98304 CAPLUS
DOCUMENT NUMBER: 132:151564
TITLE: Preparation of substituted anilides as modulators, agonists or antagonists of the CCR5 receptor
INVENTOR(S): Ku, Thomas W.; Bondinell, William E.; Neeb, Michael J.
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000006146	A1	20000210	WO 1999-US17121	19990728 <--
W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2338764	AA	20000210	CA 1999-2338764	19990728 <--

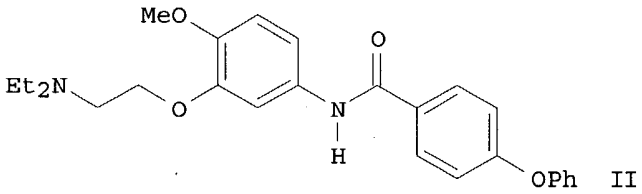
AU 9952392	A1	20000221	AU 1999-52392		19990728 <--
BR 9912406	A	20010424	BR 1999-12406		19990728
EP 1100485	A1	20010523	EP 1999-937589		19990728
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
TR 200100267	T2	20010921	TR 2001-200100267		19990728
JP 2002521436	T2	20020716	JP 2000-562001		19990728
NO 2001000446	A	20010126	NO 2001-446		20010126
PRIORITY APPLN. INFO.:			US 1998-94406P	P	19980728
			US 1999-134157P	P	19990514
			WO 1999-US17121	W	19990728

OTHER SOURCE(S): MARPAT 132:151564

GI



I



II

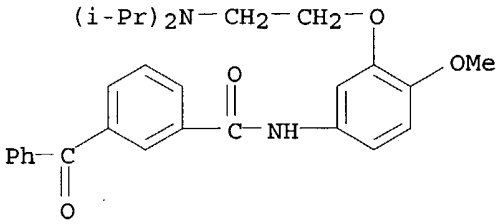
AB The title compds. [I; the basic N in moiety E may be optionally quaternized with alkyl or is optionally present as the N-oxide; P1, P2 = Ph, fused bicyclic aryl, monocyclic heterocyclyl, etc.; A = CO, O, SOc, etc.; L = CH2NH, NHCH2, etc.; R1, R2 = H, alkyl, alkenyl, etc.; R3 = H, alkyl, cycloalkyl, etc.; a, b = 1-3; c = 0-2] which are modulators, agonists or antagonists of the CCR5 receptor, and therefore useful in **treating** COPD, asthma and atopic disorders, **rheumatoid arthritis**, atherosclerosis, sarcoidosis and other fibrotic disease, psoriasis, autoimmune diseases such as multiple sclerosis, inflammatory bowel disease, and HIV, were prepared E.g., a synthesis of benzamide II starting with (4-formyl-3,5-dimethoxyphenoxy)-Merrifield resin and 3-[2-(diethylamino)ethoxy]-4-methoxyaniline, was given. Compds. I show CCR5 receptor modulator activity having IC50 values of 0.0001 to 100 μM.

IT **257616-21-0P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted anilides as modulators, agonists or antagonists of the CCR5 receptor)

RN 257616-21-0 CAPLUS

CN Benzamide, 3-benzoyl-N-[3-[2-[bis(1-methylethyl)amino]ethoxy]-4-methoxyphenyl]- (9CI) (CA INDEX NAME)

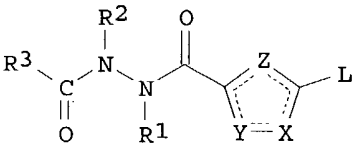


REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:819241 CAPLUS
DOCUMENT NUMBER: 132:64530
TITLE: Preparation of diacyl hydrazine compds. as protease inhibitors
INVENTOR(S): Halbert, Stacie Marie; Michaud, Evelyne; Thompson, Scott Kevin; Veber, Daniel Frank
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 167 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9966925	A1	19991229	WO 1999-US14561	19990624 <--
W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2335876	AA	19991229	CA 1999-2335876	19990624 <--
AU 9947237	A1	20000110	AU 1999-47237	19990624 <--
EP 1093367	A1	20010425	EP 1999-930779	19990624
R: BE, CH, DE, ES, FR, GB, IT, LI, NL				
JP 2002518444	T2	20020625	JP 2000-555611	19990624
PRIORITY APPLN. INFO.:			US 1998-90493P	P 19980624
			WO 1999-US14561	W 19990624

OTHER SOURCE(S): MARPAT 132:64530
GI



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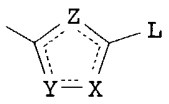


AB The present invention provides compds. I [L = C2-6 alkyl, Ar- or Het-C0-6 alkyl, CHR4NR5R6, CHR4Ar, CHR4OAr, NR4R7; X, Y, Z = N, O, S, CR10; R1, R2, R5, R10 = H, C1-6 alkyl, C2-6 alkenyl, Ar- or Het-C0-6 alkyl; R3 = C3-6 alkyl, Ar, Het, heterocycle Q, etc.; R4 = H, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, Ar- or Het-C0-6 alkyl, etc.; R6 = R14 or an acyl group such as R14CO, R14C(S), R14OCO (R14 = C1-6 alkyl, C2-6 alkenyl, Ar- or Het C0-6 alkyl); R7 = C1-6 alkyl, C1-6 alkenyl, C3-6 cycloalkyl-, Ar-, or Het-C0-6 alkyl], which inhibit proteases, including cathepsin K, pharmaceutical compns. of such compds., and methods for **treating** diseases of excessive bone loss or cartilage or matrix degradation, including osteoporosis, gingival disease, and arthritis. Thus, N-[2-[N-cyclopropyl-N-(cyclopropylmethyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(6-methyl-3-

pyridinylmethoxycarbonyl)-L-β-tert-butylalanyl]hydrazide was prepared via sequential reactions of Et 6-nicotinate, L-β-tert-butylalanine, cyclopropylamine, cyclopropylcarboxaldehyde, benzoyl isothiocyanate, and Et bromopyruvate.

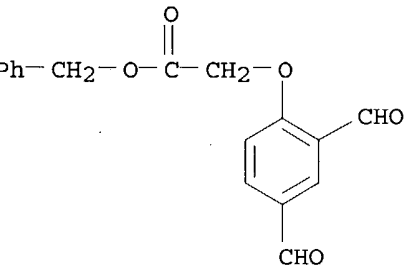
IT **250726-45-5P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of diacyl hydrazine compds. as protease inhibitors)

RN 250726-45-5 CAPLUS

CN Acetic acid, (2,4-diformylphenoxy)-, phenylmethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:753240 CAPLUS

DOCUMENT NUMBER: 132:11677

TITLE: Isolation of physiologically active VD1207 substances having a neovascularization inhibitory effect from Streptomyces strain

INVENTOR(S): Wakabayashi, Toshiaki; Kawase, Rena; Naruse, Nobuaki; Fujita, Masanori; Sameshima, Tomohiro; Watanabe, Yoshio; Dobashi, Kazuyuki; Funahashi, Yasuhiro; Senba, Taro

PATENT ASSIGNEE(S): Mercian Corporation, Japan; Eisai Co., Ltd.

SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

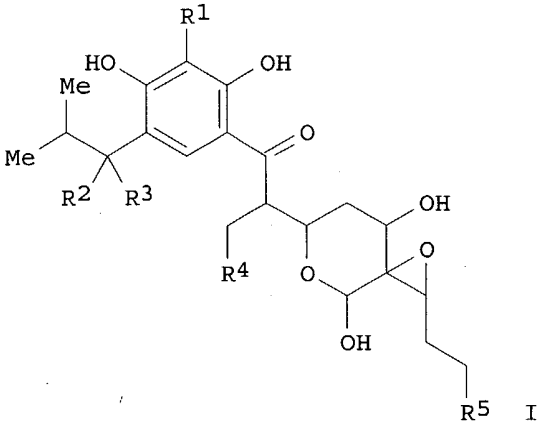
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9960000	A1	19991125	WO 1999-JP2288	19990428 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9935386	A1	19991206	AU 1999-35386	19990428 <--
EP 1081151	A1	20010307	EP 1999-917219	19990428
R: DE, FR, GB				
US 6645996	B1	20031111	US 2000-700680	20001117

PRIORITY APPLN. INFO.: JP 1998-135205 A 19980518
WO 1999-JP2288 W 19990428

OTHER SOURCE(S): MARPAT 132:11677

GI



AB The title 6-(5-isobutyl-2,4-dihydroxyphenacyl)-4,8-dihydroxy-1,5-dioxaspiro[2.5]octane compds. represented by general formula (I; R1 represents hydrogen, aldehyde or lower acyl; R2 and R3 may be the same or different and each represents hydrogen or lower alkoxy, or R2 and R3 may represent together oxygen; R4 represents lower alkyl; and R5 represents hydrogen or lower alkyl, provided that the case where R1 is aldehyde, R2 and R3 are different from each other and represent hydrogen or methoxy, R4 is Et and R5 is hydrogen is excluded) or salts thereof are isolated from a liquid culture medium of a strain belonging to the genus Streptomyces and the structures are analyzed. Also claimed are drugs based on inhibiting the expression of adhesion mols. VCAM-1 or/and E-selectin containing I as the active ingredients. These compds. are useful for the **treatment** and prevention of **rheumatoid arthritis**, solid tumor, atherosclerosis, diabetic retinopathy, vascular tumors, and psoriasis. Thus, Streptomyces sp. VD1207 was aerobically cultured in a medium containing glycerol 2, glucose 2, soybean meal 2, yeast extract 0.5, NaCl 0.25, CaCO3 0.32, CuSO4.5H2O 0.0005, MnCl2.4H2O 0.0005, and ZnSO4.7H2O 0.0005% at 28° for 64 h (2 culture tanks each containing 100 L medium) and centrifuged to remove the bacteria followed by chromatog. separation using a Diaion HP-20 column, a YMC-GEL ODS-AM 120-S50 column and silica gel chromatog., HPLC separation, or thin layer chromatog. to give VD1207U1 [(+)-I; R1 = R5 = H, R2R3 = O, R4 = Et], VD1207U2 [(-)-I; R1 = R5 = H, R2R3 = O, R4 = Et], VD1207A1 [(+)-I; R1 = R5 = H, R2R3 = O, R4 = i-Pr], VD1207A2 [(-)-I; R1 = R5 = H, R2R3 = O, R4 = i-Pr], VD1207B [(-)-I; R1 = CHO; R2, R3 = OMe, H; R4 = Et, R5 = H], VD1207C [(+)-I; R1 = CHO; R2, R3 = OMe, H; R4 = Et, R5 = H], VD1207D [(-)-I; R1 = CHO, R2 = R3 = R5 = H, R4 = Et], VD1207E [(-)-I; R1 = CHO; R2, R3 = OMe, H; R4 = i-Pr, R5 = H], VD1207F [(+)-I; R1 = CHO; R2, R3 = OMe, H; R4 = i-Pr, R5 = H], VD1207F' [(+)-I; R1 = CHO; R2, R3 = OMe, H; R4 = n-Pr, R5 = H], VD1207G' [(-)-I; R1 = CHO, R2 = R3 = R5 = H, R4 = n-Pr], VD1207G1 [(-)-I; R1 = CHO, R2 = R3 = H, R4 = Et, R5 = Me], VD1207G2 [(+)-I; R1 = CHO, R2 = R3 = R5 = H, R4 = i-Pr], and VD1207H [(-)-I; R1 = COMe, R2 = R3 = R5 = H, R4 = Et]. In a neovascularization inhibitory assay, VD1207 A2, B, C, D, E, F, F', G1, G2, G', and H in vitro showed IC50 of 1, 0.053, 0.050, 0.019, 0.047, 0.067, 0.10, 0.070, 0.034, 0.11, and 0.38 μg/mL, resp., for inhibiting the formation of capillary vessel in rat aorta cultured in collagen.

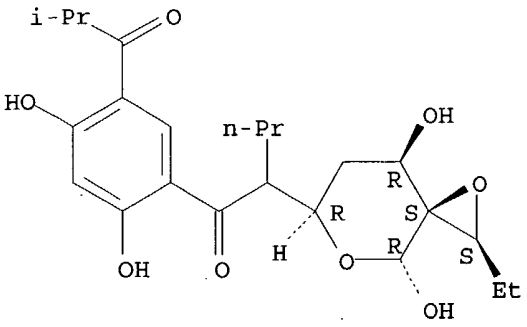
IT **251449-85-1P**, VD 1207U1 **251449-86-2P**, VD 1207U2
251449-87-3P, VD 1207A1 **251449-88-4P**, VD 1207A2
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(isolation of physiol. active VD1207 substances having neovascularization inhibitory effect from Streptomyces sp. VD1207)

RN 251449-85-1 CAPLUS

CN 1-Pentanone, 1-[2,4-dihydroxy-5-(2-methyl-1-oxopropyl)phenyl]-2-[(2S,3S,4R,8R)-2-ethyl-4,8-dihydroxy-1,5-dioxaspiro[2.5]oct-6-yl]- (9CI) (CA INDEX NAME)

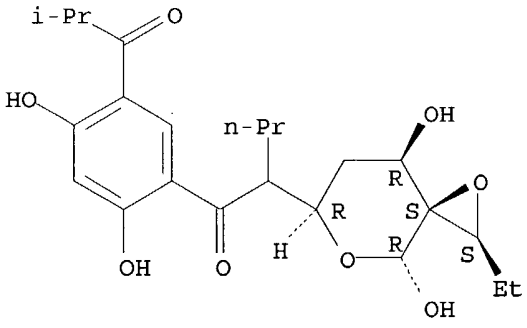
Absolute stereochemistry. Rotation (+).

Currently available stereo shown.



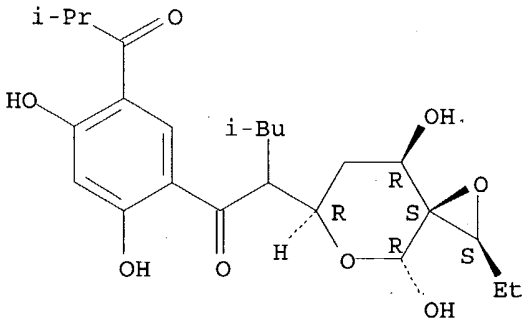
RN 251449-86-2 CAPLUS
CN 1-Pentanone, 1-[2,4-dihydroxy-5-(2-methyl-1-oxopropyl)phenyl]-2-[(2S,3S,4R,8R)-2-ethyl-4,8-dihydroxy-1,5-dioxaspiro[2.5]oct-6-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Currently available stereo shown.



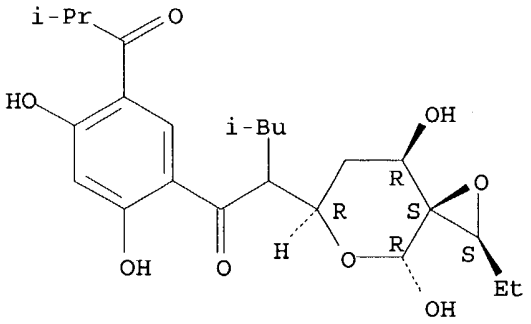
RN 251449-87-3 CAPLUS
CN 1-Pentanone, 1-[2,4-dihydroxy-5-(2-methyl-1-oxopropyl)phenyl]-2-[(2S,3S,4R,8R)-2-ethyl-4,8-dihydroxy-1,5-dioxaspiro[2.5]oct-6-yl]-4-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Currently available stereo shown.



RN 251449-88-4 CAPLUS
CN 1-Pentanone, 1-[2,4-dihydroxy-5-(2-methyl-1-oxopropyl)phenyl]-2-[(2S,3S,4R,8R)-2-ethyl-4,8-dihydroxy-1,5-dioxaspiro[2.5]oct-6-yl]-4-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Currently available stereo shown.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 10 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:753058 CAPLUS
DOCUMENT NUMBER: 132:426
TITLE: Diacyl carbohydrazide compds. as protease inhibitors for **treating** diseases of excessive bone loss or cartilage or matrix degradation
INVENTOR(S): Halbert, Stacie Marie; Thompson, Scott Kevin; Veber, Daniel Frank
PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9959570	A1	19991125	WO 1998-US17275	19980820 <--
W: AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, HU, ID, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2332492	AA	19991125	CA 1998-2332492	19980820 <--
AU 9891102	A1	19991206	AU 1998-91102	19980820 <--
EP 1079821	A1	20010307	EP 1998-943273	19980820
R: BE, CH, DE, ES, FR, GB, IT, LI, NL				
JP 2002515428	T2	20020528	JP 2000-549235	19980820

PRIORITY APPLN. INFO.: US 1998-86553P P 19980521
WO 1998-US17275 W 19980820

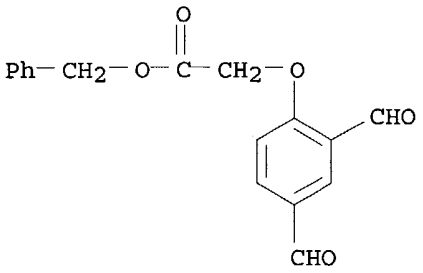
OTHER SOURCE(S): MARPAT 132:426

AB The present invention provides diacyl carbohydrazide compds., and pharmaceutically acceptable salts, hydrates and solvates thereof, which inhibit proteases, including cathepsin K, pharmaceutical compns. of such compds., novel intermediates of such compds., and methods for **treating** diseases of excessive bone loss or cartilage or matrix degradation, including osteoporosis; gingival disease including gingivitis and periodontitis; arthritis, more specifically, **osteoarthritis** and **rheumatoid arthritis**; Paget's disease; hypercalcemia of malignancy; and metabolic bone disease, comprising inhibiting said bone loss or excessive cartilage or matrix degradation by administering to a patient in need thereof a compound of the present invention.

IT **250726-45-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(diacyl carbohydrazide compds. as protease inhibitors for **treating** diseases of excessive bone loss or cartilage or matrix degradation)

RN 250726-45-5 CAPLUS

CN Acetic acid, (2,4-diformylphenoxy)-, phenylmethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:753019 CAPLUS
DOCUMENT NUMBER: 132:12506
TITLE: Preparation of peptides for **treating** diseases of excessive bone loss or cartilage or matrix degradation as cysteine protease inhibitors
INVENTOR(S): Bondinell, William Edward; Desjarlais, Renee Louise; Veber, Daniel Frank; Yamashita, Dennis Shinji
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 128 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 9959526	A2	19991125	WO 1999-US11266		19990520	<--
WO 9959526	A3	20000120				
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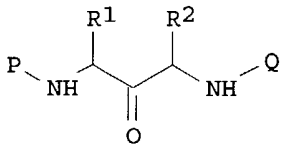
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG						
CA 2332531	AA	19991125	CA 1999-2332531		19990520	<--
EP 1067894	A2	20010117	EP 1999-924421		19990520	
R: BE, CH, DE, ES, FR, GB, IT, LI, NL						
JP 2002515411	T2	20020528	JP 2000-549192		19990520	
US 6518267	B1	20030211	US 2000-700828		20001121	
PRIORITY APPLN. INFO.:			US 1998-86557P	P	19980521	
			WO 1999-US11266	W	19990520	

OTHER SOURCE(S): MARPAT 132:12506
GI



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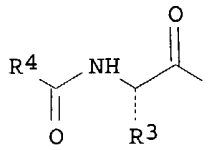
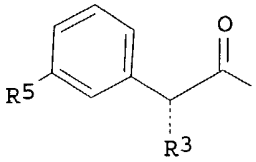
X = 

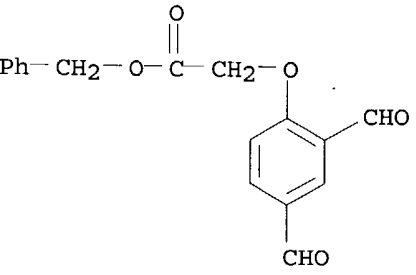
Y = 

AB The present invention provides peptides bis-aminomethyl carbonyl protease inhibitors I (R1, R2 = alkyl; P = X, Y; R3 selected from the group consisting of: CH2CH(CH3)2, CH2CH2CH3, CH2CH=CH2, or CH2Ph; R4 is selected from the group consisting of alkyl; N-piperazine; N-tetrahydroisoquinoline; substituted alkyl, Ph, benzofuran, benzothiazole; quinoline; naphthyl; and benzoxazole; R5 = Ph and Ph substituted with alkyl, N-piperidine, benzofuran; pyridine; Q = arylacyl) and pharmaceutically acceptable salts, hydrates and solvates thereof which inhibit proteases, including cathepsin K, pharmaceutical compns. of such compds., and methods for **treating** diseases of excessive bone loss or cartilage or matrix degradation, including osteoporosis; gingival disease including gingivitis and periodontitis; arthritis, more specifically, **osteoarthritis** and **rheumatoid arthritis**; Paget's disease; hypercalcemia of malignancy; and metabolic bone disease, comprising inhibiting said bone loss or excessive cartilage or matrix degradation by administering to a patient in need thereof a compound of the present invention. Thus, (S)-3N-(N-(thianaphthenyl-2-carbonyl)-leucinyl)-amino-1N-(3-{2-(1-oxo)-pyridyl}phenylacetyl)-amino-butan-2-one was prepared for **treating** diseases of excessive bone loss or cartilage or matrix degradation as cysteine protease inhibitor. Determination of cathepsin K proteolytic catalytic activity of these compds. are reported.

IT **250726-45-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptides for **treating** diseases of excessive bone loss or cartilage or matrix degradation as cysteine protease inhibitors)

RN 250726-45-5 CAPLUS

CN Acetic acid, (2,4-diformylphenoxy)-, phenylmethyl ester (9CI) (CA INDEX NAME)



L6 ANSWER 12 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:566043 CAPLUS

DOCUMENT NUMBER: 131:199620

TITLE: Preparation of indole derivatives as phospholipase enzyme inhibitors

INVENTOR(S): Seehra, Jasbir S.; Xiang, Yibin; Bemis, Jean; McKew, John; Kaila, Neelu; Chen, Lihren

PATENT ASSIGNEE(S): Genetics Institute, Inc., USA

SOURCE: PCT Int. Appl., 225 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9943672	A1	19990902	WO 1999-US3388	19990217 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2322163	AA	19990902	CA 1999-2322163	19990217 <--
AU 9932970	A1	19990915	AU 1999-32970	19990217 <--
BR 9909242	A	20001114	BR 1999-9242	19990217 <--
TR 200002445	T2	20001221	TR 2000-200002445	19990217 <--
EP 1062216	A1	20001227	EP 1999-936073	19990217 <--
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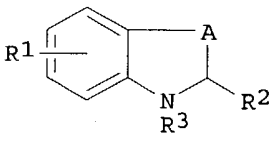
NO 2000004217	A	20001023	NO 2000-4217	20000823 <--
BG 104781	A	20011031	BG 2000-104781	20000919

PRIORITY APPLN. INFO.:
US 1998-30102 A 19980225
WO 1999-IS3388 W 19990217
WO 1999-US3388 W 19990217

OTHER SOURCE(S): MARPAT 131:199620
GI



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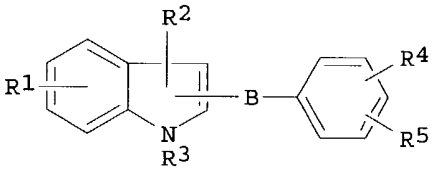

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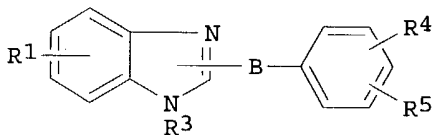

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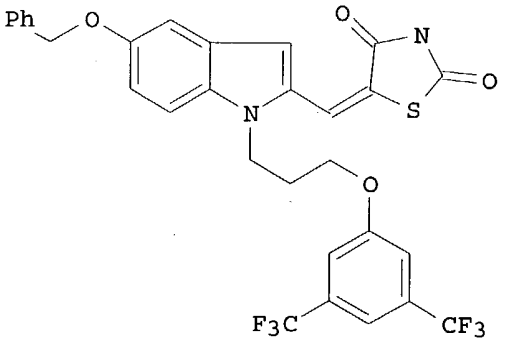


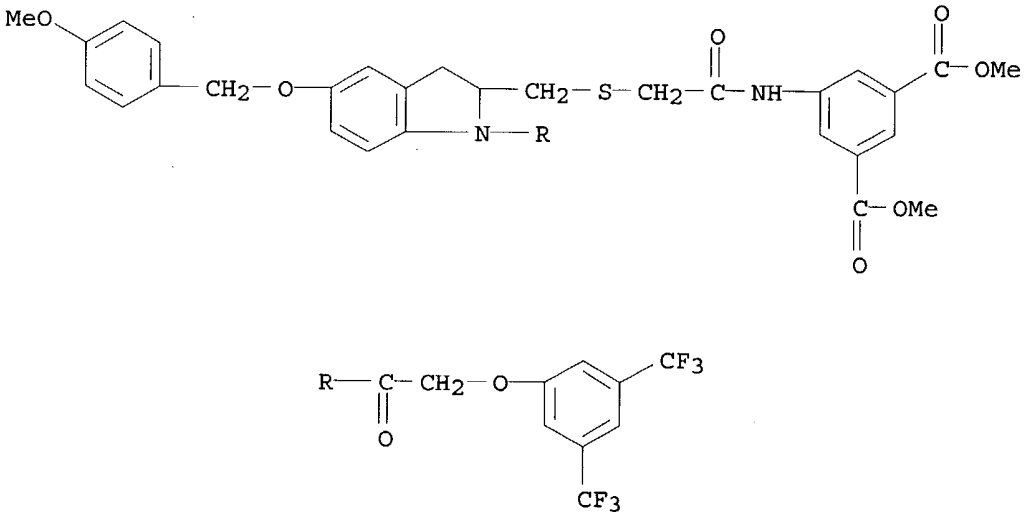
IV

AB Indole derivs. (I), (II), and (III) [where A = CH2 or CH2CH2; B = (CH2)n, (CH2O)n, (CH2S)n, (OCH2)n, (SCH2)n, (CH=CH)n, (C.tplbond.C)n, CON(R6), N(R6)CO, O, S, or N(R6); R1 and R5 = independently H, OH, halogen, CN, NO2, C1-5 alkyl, alkenyl, alkynyl, or (un)substituted aryl, etc.; R2 and

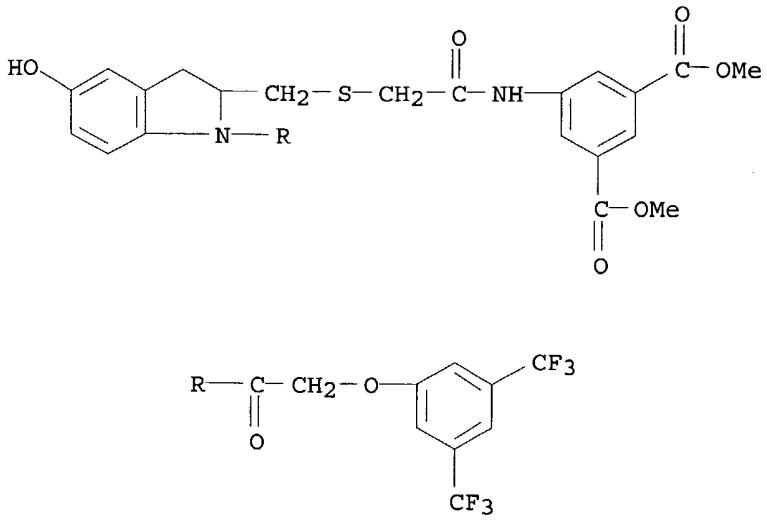
R3 = independently H, CO2H, COR5, CONR5R6, (CH2)nW(CH2)mZR5, (CH2)nWR5, ZR5, C1-10 alkyl, alkenyl, or substituted aryl; R4 = H, OH, OR6, SR6, CN, COR6, NHR6, CO2H, COR6R7, NO2, (un)substituted sulfamidocarbonyl, C1-5 alkyl, alkenyl, or substituted aryl; R6, R7 = H, C1-5 alkyl, alkenyl, alkynyl, or (un)substituted aryl; W = O, S, CH2, CH=CH, C.tplbond.C, or N(R6); X = O, S, N(R6); Z = CH2, O, S, N(R6), CO, CON(R6), N(R6)CO; m and n = independently 0-4] and pharmaceutically acceptable salts thereof, were prepared Thus, 2,4-thiazolidinedione and K2CO3 followed by NaOH were added to 5-(benzyloxyl)-1-(4-{[3,5-bis(trifluoromethyl)phenoxy]methyl}benzyl)-1H-indole-2-carboxaldehyde in EtOH to form the 2,4-thiazolidinedion-4-ylidene derivative The ylidene was dissolved in a solution of DMF and NaH, reacted with an alkyl ester of 4-(bromomethyl)benzoic acid, and deesterified with HF to yield the acid, (E)-(IV). The title compds. are useful as phospholipase enzyme inhibitors, especially cytosolic phospholipase A2 (cPLA2), for **treatment** of inflammatory conditions, particularly where inhibition of production of prostaglandins, leukotrienes, and PAF are all desired. Eighty-seven compds. of the invention were tested for phospholipase enzyme inhibiting activity in the LysoPC and/or Coumarine assay. IC50 values ranged from 0.081 μM to >50 μM for the LysoPC assay and from 2.5 μM to >64 μM for the Coumarine assay. Selected compds. were tested for in vivo activity in the carrageenan-induced rat paw edema test, and showed 4.2% to 34.2% inhibition. Forty-eight compds. of the invention were tested for cPLA2 enzyme activity, and exhibited 25% to 95% inhibition at concns. of 3 μM to 100 μM.

IT **204017-40-3P 204017-41-4P 204017-42-5P**
204017-63-0P 204017-64-1P 204017-65-2P
204017-75-4P 204017-76-5P 204017-77-6P
241490-04-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of indole derivs. as phospholipase enzyme inhibitors for **treatment** of inflammatory conditions)

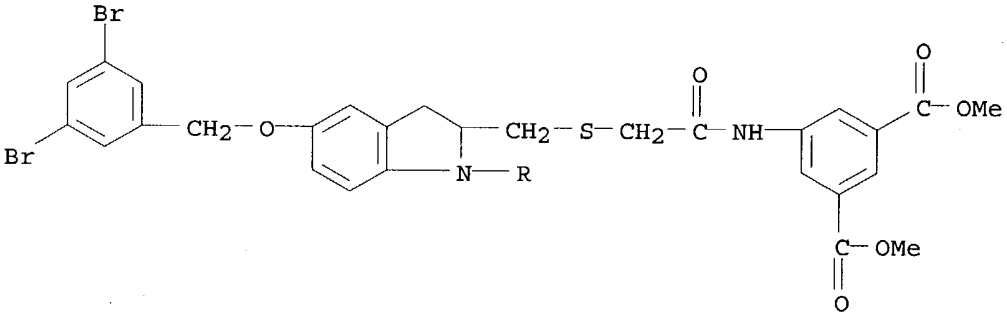
RN 204017-40-3 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-[[[[[1-[[3,5-bis(trifluoromethyl)phenoxy]acetyl]-2,3-dihydro-5-[(4-methoxyphenyl)methoxy]-1H-indol-2-yl]methyl]thio]acetyl]amino]-, dimethyl ester (9CI) (CA INDEX NAME)

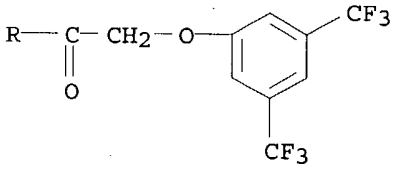


RN 204017-41-4 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-[[[[[1-[[3,5-bis(trifluoromethyl)phenoxy]acetyl]-2,3-dihydro-5-hydroxy-1H-indol-2-yl]methyl]thio]acetyl]amino]-, dimethyl ester (9CI) (CA INDEX NAME)

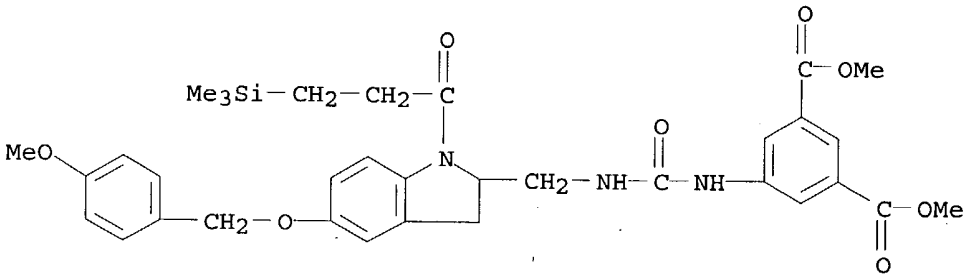


RN 204017-42-5 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-[[[[[1-[[3,5-bis(trifluoromethyl)phenoxy]acetyl]-5-[(3,5-dibromophenyl)methoxy]-2,3-dihydro-1H-indol-2-yl]methyl]thio]acetyl]amino]-, dimethyl ester (9CI) (CA INDEX NAME)



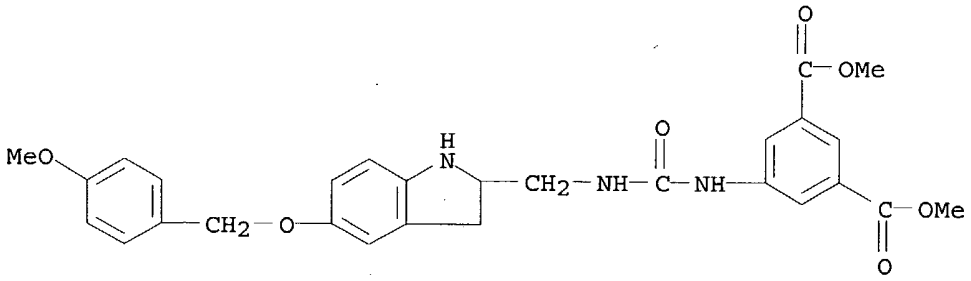


RN 204017-63-0 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-[[[[[2,3-dihydro-5-[(4-methoxyphenyl)methoxy]-1-[1-oxo-3-(trimethylsilyl)propyl]-1H-indol-2-yl]methyl]amino]carbonyl]amino]-, dimethyl ester (9CI) (CA INDEX NAME)

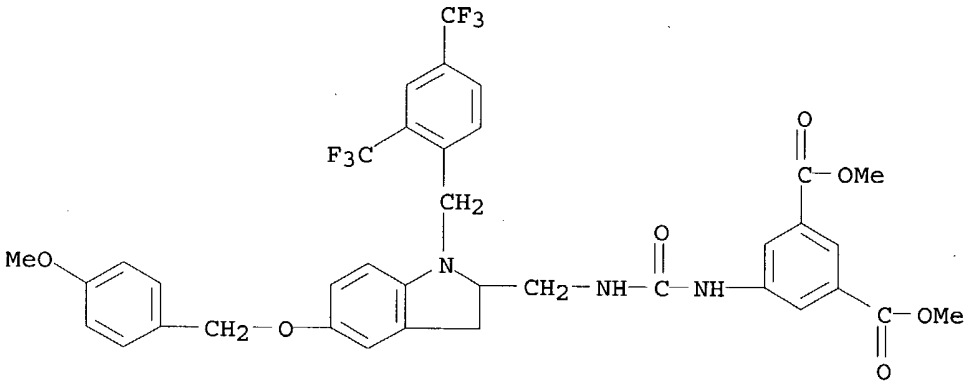


RN 204017-64-1 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-[[[[[2,3-dihydro-5-[(4-

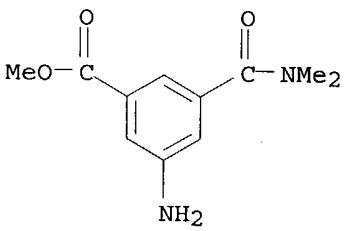
methoxyphenyl)methoxy]-1H-indol-2-yl]methyl]amino]carbonyl]amino]-, dimethyl ester (9CI) (CA INDEX NAME)



RN 204017-65-2 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-[[[[[1-[[2,4-bis(trifluoromethyl)phenyl]methyl]-2,3-dihydro-5-[(4-methoxyphenyl)methoxy]-1H-indol-2-yl]methyl]amino]carbonyl]amino]-, dimethyl ester (9CI) (CA INDEX NAME)



RN 204017-75-4 CAPLUS
CN Benzoic acid, 3-amino-5-[(dimethylamino)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



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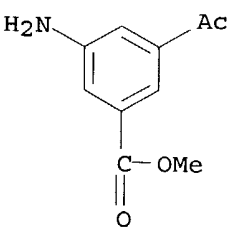
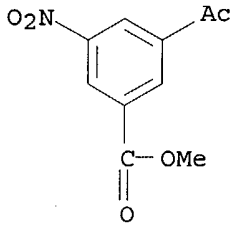
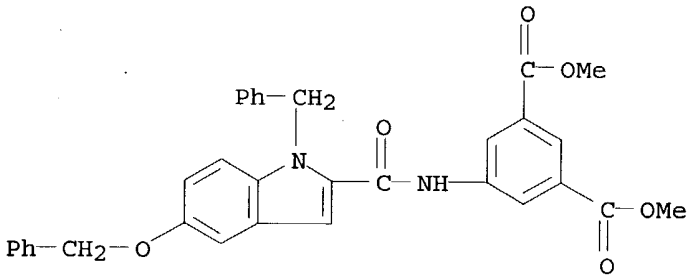
CN Benzoic acid, 3-acetyl-5-amino-, methyl ester (9CI) (CA INDEX NAME)



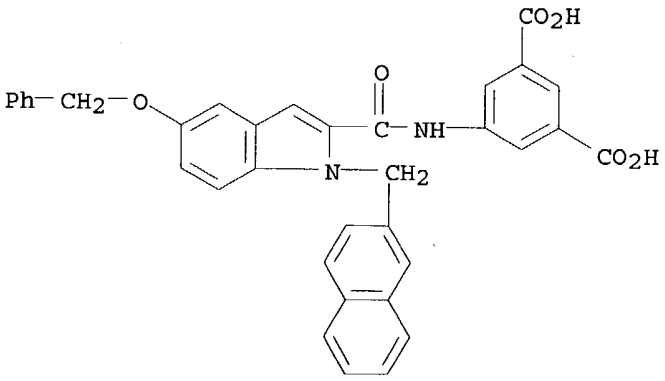
RN 204017-77-6 CAPLUS
CN Benzoic acid, 3-acetyl-5-nitro-, methyl ester (9CI) (CA INDEX NAME)



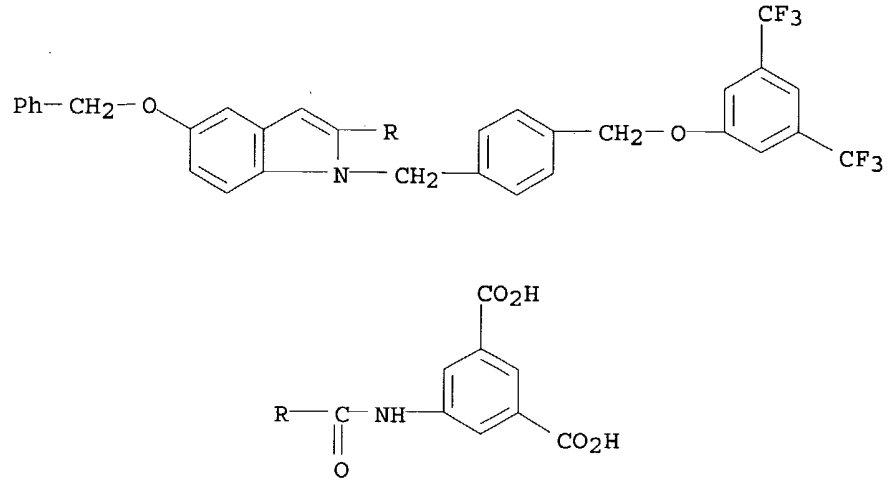
RN 241490-04-0 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-[[[5-(phenylmethoxy)-1-(phenylmethyl)-1H-indol-2-yl]carbonyl]amino]-, dimethyl ester (9CI) (CA INDEX NAME)



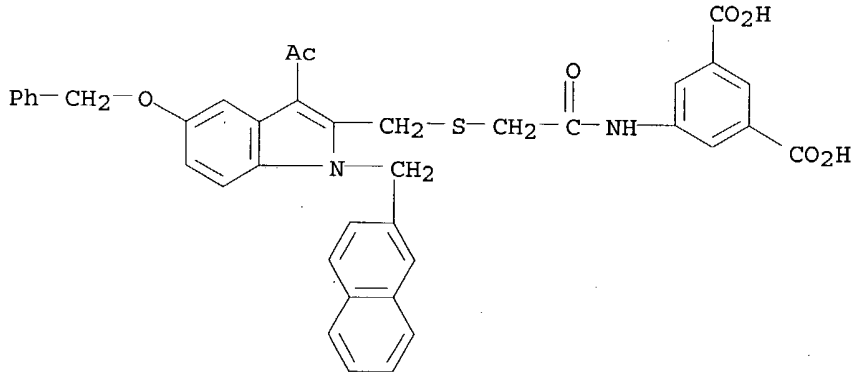
IT **204016-33-1P 204016-35-3P 204016-42-2P**
204016-45-5P 204016-64-8P 204016-65-9P
204016-66-0P 204016-69-3P 204017-09-4P
204017-12-9P 204017-13-0P 241489-80-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of indole derivs. as phospholipase enzyme inhibitors for **treatment** of inflammatory conditions)
RN 204016-33-1 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-[[[1-(2-naphthalenylmethyl)-5-(phenylmethoxy)-1H-indol-2-yl]carbonyl]amino]- (9CI) (CA INDEX NAME)



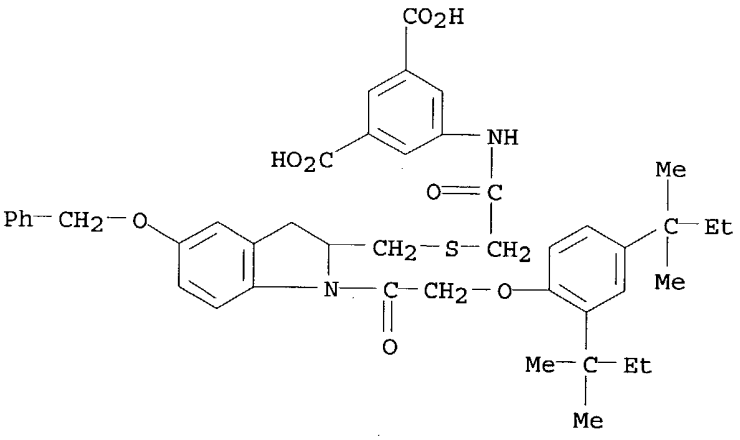
RN 204016-35-3 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-[[[1-[[4-[[3,5-bis(trifluoromethyl)phenoxy]methyl]phenyl]methyl]-5-(phenylmethoxy)-1H-indol-2-yl]carbonyl]amino]- (9CI) (CA INDEX NAME)



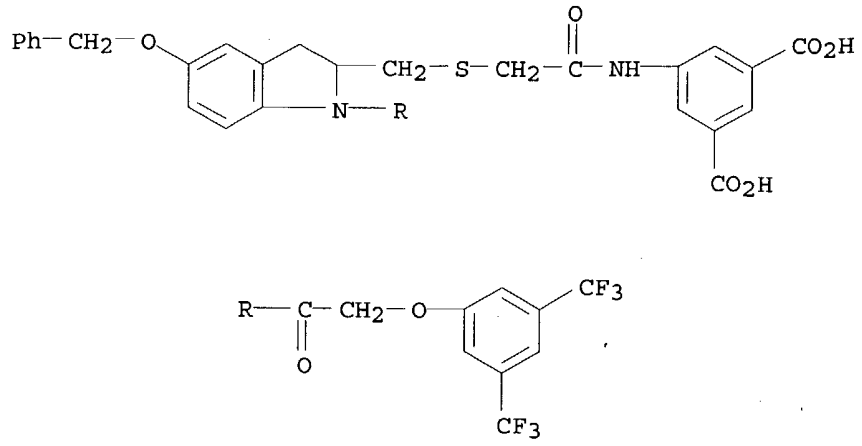
RN 204016-42-2 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-[[[[[3-acetyl-1-(2-naphthalenylmethyl)-5-(phenylmethoxy)-1H-indol-2-yl]methyl]thio]acetyl]amino]- (9CI) (CA INDEX NAME)



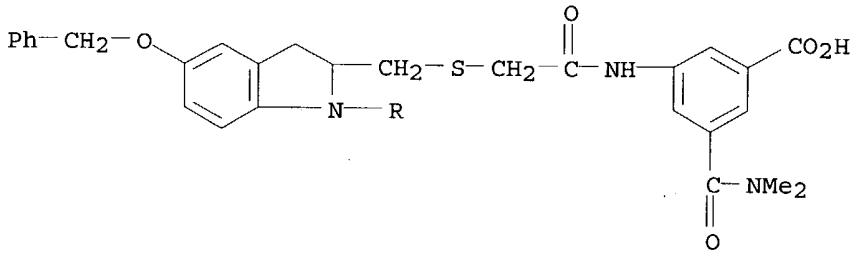
RN 204016-45-5 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-[[[[[1-[[2,4-bis(1,1-dimethylpropyl)phenoxy]acetyl]-2,3-dihydro-5-(phenylmethoxy)-1H-indol-2-yl]methyl]thio]acetyl]amino]- (9CI) (CA INDEX NAME)

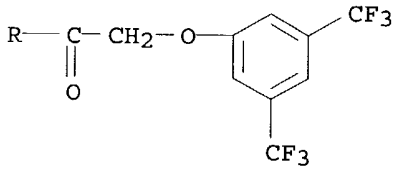


RN 204016-64-8 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-[[[[[1-[[3,5-bis(trifluoromethyl)phenoxy]acetyl]-2,3-dihydro-5-(phenylmethoxy)-1H-indol-2-yl]methyl]thio]acetyl]amino]- (9CI) (CA INDEX NAME)



RN 204016-65-9 CAPLUS
CN Benzoic acid, 3-[[[[[1-[[3,5-bis(trifluoromethyl)phenoxy]acetyl]-2,3-dihydro-5-(phenylmethoxy)-1H-indol-2-yl]methyl]thio]acetyl]amino]-5-[(dimethylamino)carbonyl]- (9CI) (CA INDEX NAME)





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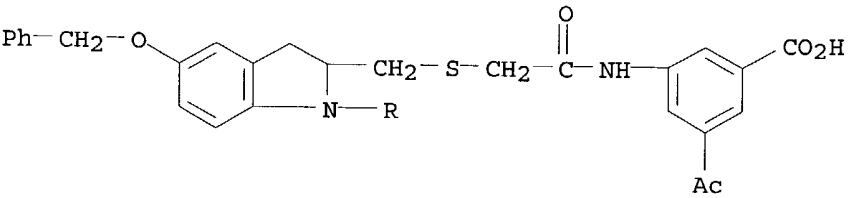
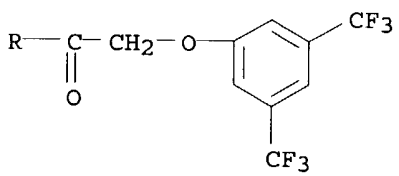
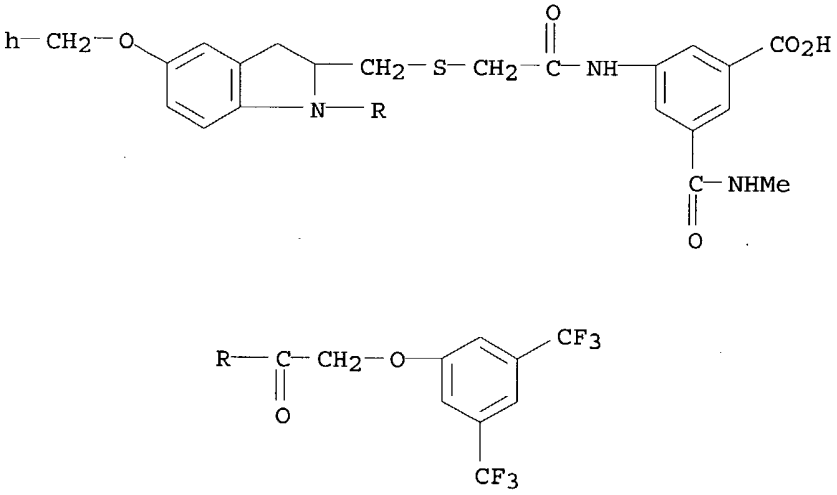
CN Benzoic acid, 3-acetyl-5-[[[[[1-[[3,5-bis(trifluoromethyl)phenoxy]acetyl]-2,3-dihydro-5-(phenylmethoxy)-1H-indol-2-yl]methyl]thio]acetyl]amino]- (9CI) (CA INDEX NAME)

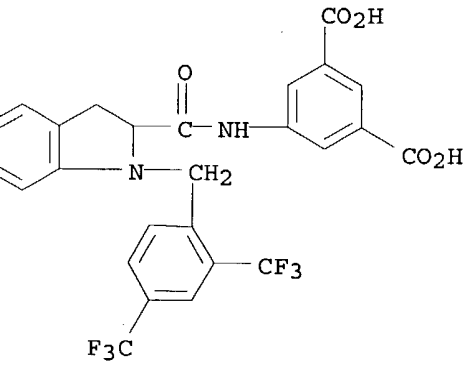




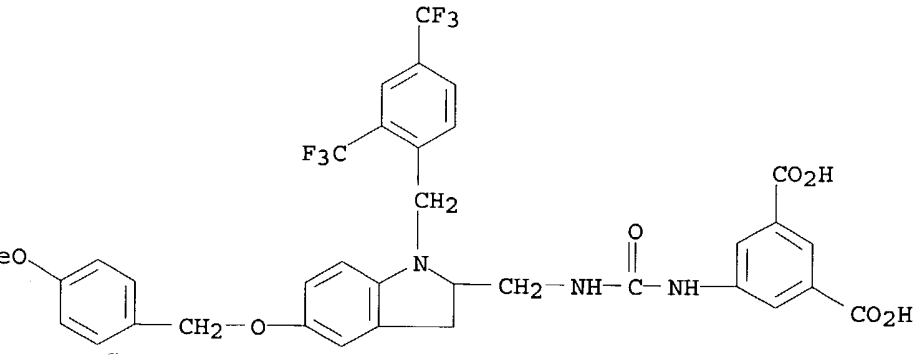
LN 204016-69-3 CAPLUS
'N Benzoic acid, 3-[[[[[1-[[3,5-bis(trifluoromethyl)phenoxy]acetyl]-2,3-dihydro-5-(phenylmethoxy)-1H-indol-2-yl]methyl]thio]acetyl]amino]-5-[(methylamino)carbonyl]- (9CI) (CA INDEX NAME)



N 204017-09-4 CAPLUS
N 1,3-Benzenedicarboxylic acid, 5-[[[1-[[2,4-bis(trifluoromethyl)phenyl]methyl]-2,3-dihydro-1H-indol-2-yl]carbonyl]amino]- (9CI) (CA INDEX NAME)

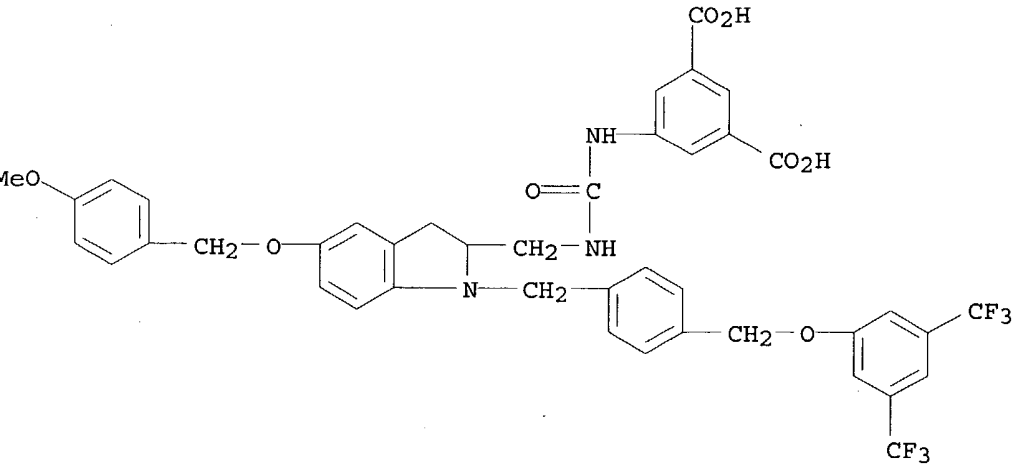


N 204017-12-9 CAPLUS
N 1,3-Benzenedicarboxylic acid, 5-[[[[[1-[[2,4-bis(trifluoromethyl)phenyl]methyl]-2,3-dihydro-5-[(4-methoxyphenyl)methoxy]-1H-indol-2-yl]methyl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

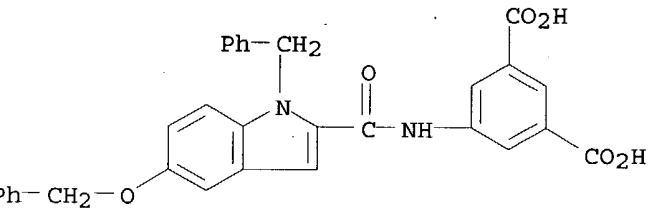


N 204017-13-0 CAPLUS
N 1,3-Benzenedicarboxylic acid, 5-[[[[[1-[[4-[[3,5-

bis(trifluoromethyl)phenoxy]methyl]phenyl]methyl]-2,3-dihydro-5-[(4-methoxyphenyl)methoxy]-1H-indol-2-yl]methyl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)



RN 241489-80-5 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-[[[5-(phenylmethoxy)-1-(phenylmethyl)-1H-indol-2-yl]carbonyl]amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:566026 CAPLUS
DOCUMENT NUMBER: 131:199619
TITLE: Preparation of indole derivatives as phospholipase enzyme inhibitors
INVENTOR(S): Seehra, Jasbir S.; Mckew, John C.; Lovering, Frank; Bemis, Jean E.; Xiang, Yibin; Chen, Lihren; Knopf, John L.
PATENT ASSIGNEE(S): Genetics Institute, Inc., USA
SOURCE: PCT Int. Appl., 182 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9943654	A2	19990902	WO 1999-US3898	19990224 <--
WO 9943654	A3	19991028		

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CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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BG 104779	A	20011031	BG 2000-104779		20000919
PRIORITY APPLN. INFO.:			US 1998-30592	A	19980225
			WO 1999-US3898	W	19990224

OTHER SOURCE(S): MARPAT 131:199619

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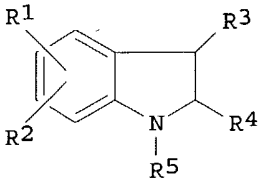

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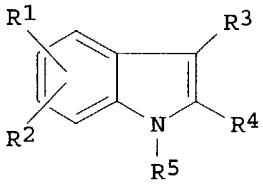

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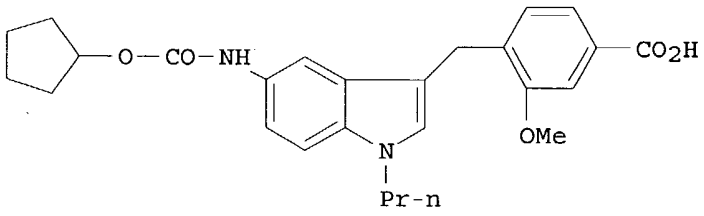


III

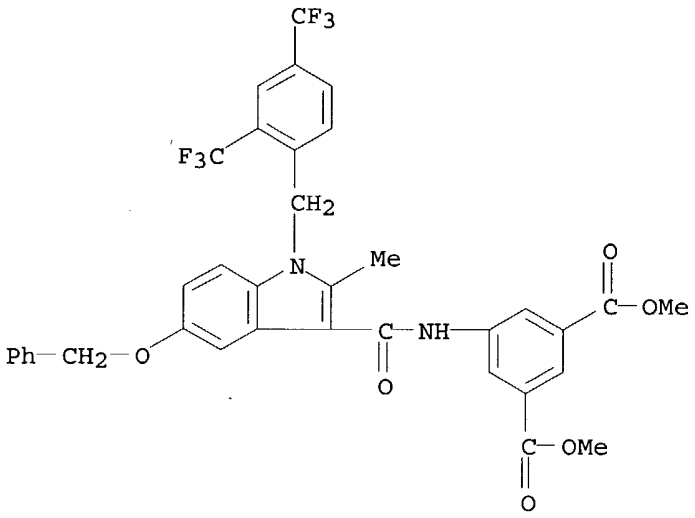
AB Indole derivs. (I) and (II) [where R1 = H, halogen, CF3, C1-10 alkyl, S-C1-10 alkyl, C1-10 alkoxy, CN, NO2, NH2, Ph, OPh, SPh, CH2Ph, OCH2Ph, SCH2Ph, or (un)substituted amido, carbamido, sulfonyl, etc.; R2 = H, halogen, CF3, OH, C1-10 alkyl, C1-10 alkoxy, CHO, CN, NO2, (un)substituted amino, SO2-C1-6 alkyl; R3 = (un)substituted carboxylic acid, OPO3H2, SO3H, etc.; R4 = H, CF3, C1-6 alkyl, C1-6 alkoxy, (C1-6 alkyl)cycloalkyl, CHO, halogen, etc.; R5 = C1-6 alkyl, C1-6 alkoxy, (C1-6 alkyl)cycloalkyl, etc.] and pharmaceutically acceptable salts thereof, were prepared by several methods. Thus, 5-nitroindole was C3-alkylated with Me 4-(bromomethyl)-3-methoxybenzoate in dioxane, N-alkylated with 1-iodopropane in a solution of THF and NaH, and converted to the amine by hydrogenation over Pt/C. The amine was converted to the carbamate by addition of cyclopentyl chloroformate in CH2Cl2 and 4-methylmorpholine and the resultant ester hydrolyzed to yield 4-[(5-{[(cyclopentyloxy)carbonyl]amino}-1-propyl-1H-indol-3-yl)methyl]-3-methoxybenzoic acid (III). The title compds. are useful as phospholipase enzyme inhibitors, especially cytosolic phospholipase A2 (cPLA2), for **treatment** of inflammatory conditions, particularly where inhibition of production of prostaglandins, leukotrienes, and PAF are all desired. Over one hundred compds. of the invention were tested for cPLA2 inhibiting activity in the Coumarine assay and rat carrageenan-induced footpad edema test. Compds. exhibited 7% to 98% inhibition at concns. of 0.125 μM to 400 μM in the Coumarine assay and -7.16% to 34.52% inhibition at concns. of 2 μM to 20 μM in the footpad edema test.

IT **241498-37-3P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

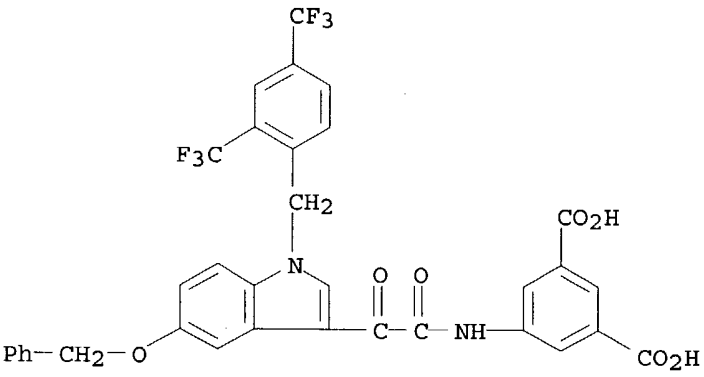
(intermediate; preparation of indole derivs. as phospholipase enzyme inhibitors for **treatment** of inflammatory conditions)

RN 241498-37-3 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-[[[1-[[2,4-bis(trifluoromethyl)phenyl]methyl]-2-methyl-5-(phenylmethoxy)-1H-indol-3-yl]carbonyl]amino]-, dimethyl ester (9CI) (CA INDEX NAME)

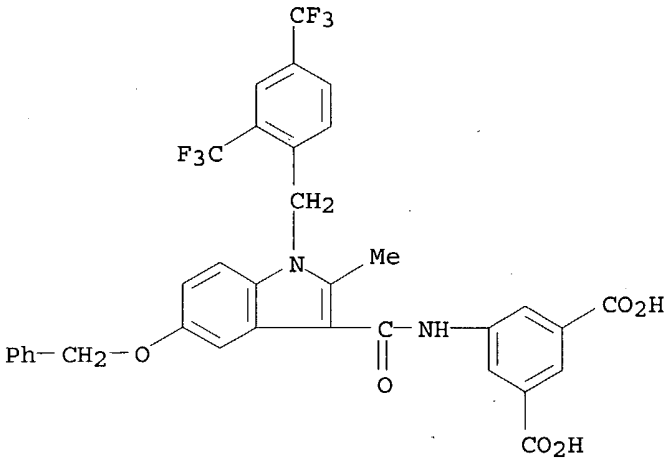


IT **241497-45-0P 241497-83-6P 241497-85-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of indole derivs. as phospholipase enzyme inhibitors for **treatment** of inflammatory conditions)

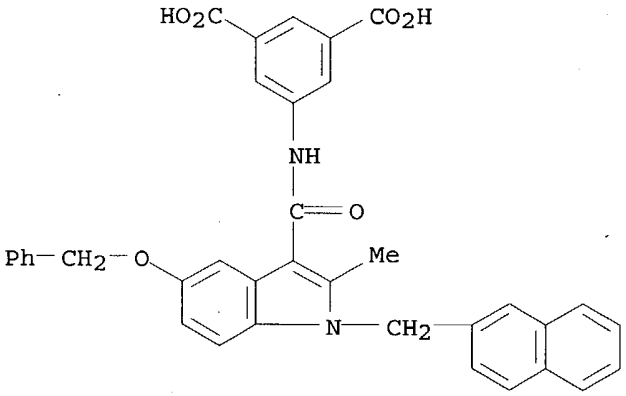
RN 241497-45-0 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-[[[1-[[2,4-bis(trifluoromethyl)phenyl]methyl]-5-(phenylmethoxy)-1H-indol-3-yl]oxoacetyl]amino]- (9CI) (CA INDEX NAME)



RN 241497-83-6 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-[[[1-[[2,4-bis(trifluoromethyl)phenyl]methyl]-2-methyl-5-(phenylmethoxy)-1H-indol-3-yl]carbonyl]amino]- (9CI) (CA INDEX NAME)



RN 241497-85-8 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-[[[2-methyl-1-(2-naphthalenylmethyl)-5-(phenylmethoxy)-1H-indol-3-yl]carbonyl]amino]- (9CI) (CA INDEX NAME)



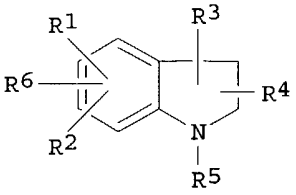
L6 ANSWER 14 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:566023 CAPLUS
DOCUMENT NUMBER: 131:199618
TITLE: Preparation of indole derivatives as phospholipase enzyme inhibitors
INVENTOR(S): Seehra, Jasbir S.; Kaila, Neelu; McKew, John C.; Lovering, Frank; Bemis, Jean E.; Xiang, Yibin
PATENT ASSIGNEE(S): Genetics Institute, Inc., USA
SOURCE: PCT Int. Appl., 128 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9943651	A2	19990902	WO 1999-US3899	19990224 <--
WO 9943651	A3	19991216		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2322161	AA	19990902	CA 1999-2322161	19990224 <--

AU 9927826	A1	19990915	AU 1999-27826		19990224 <--
BR 9908280	A	20001031	BR 1999-8280		19990224 <--
EP 1056719	A2	20001206	EP 1999-908379		19990224 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI					
TR 200002446	T2	20001221	TR 2000-200002446		19990224 <--
JP 2002504539	T2	20020212	JP 2000-533409		19990224
EE 200000486	A	20020215	EE 2000-486		19990224
NO 2000004220	A	20001005	NO 2000-4220		20000823 <--
HR 2000000552	A1	20010430	HR 2000-552		20000824
BG 104780	A	20011031	BG 2000-104780		20000919
US 2003153751	A1	20030814	US 2002-75079		20020508
PRIORITY APPLN. INFO.:			US 1998-30062	A	19980225
			US 1998-100426P	P	19980225
			US 1999-256413	B2	19990224
			WO 1999-US3899	W	19990224
			US 2000-677006	B1	20000929

OTHER SOURCE(S): MARPAT 131:199618

GI



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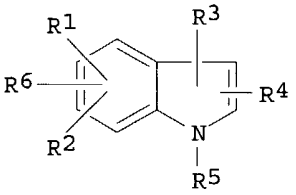
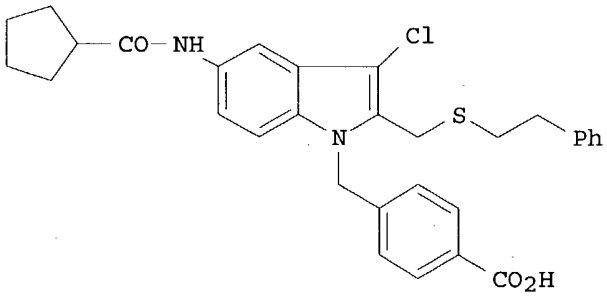


II



III

AB Indole derivs. (I) and (II) [where R1 and R6 = H, halogen, CF3, OH, C1-10 alkyl, S-C1-10 alkyl, C1-10 alkoxy, CN, NO2, Ph, OPh, SPh, CH2Ph, OCH2Ph, SCH2Ph, or (un)substituted amino, amido, carbamido, sulfonyl, etc.; R2 = H, halogen, CF3, OH, C1-10 alkyl, C1-10 alkoxy, CHO, CN, NO2, (un)substituted amino, SO2-C1-6 alkyl; R3 = H, CF3, C1-6 alkyl, C1-6 alkoxy, (C1-6 alkyl)cycloalkyl, etc.; R4 = C1-6 alkyl, C1-6 alkoxy, alkylcycloalkyl, acyl, etc.; R5 = (un)substituted carboxylic acid, OPO3H2, SO3H, etc.] and pharmaceutically acceptable salts thereof, were prepared by several methods. Thus, Et 5-nitroindole-2-carboxylate was C3-chlorinated in DMF. The alc. was formed by reduction of the ester in a two-step process and was then TBDMS-protected. The TBDMS-protected alc. was N-alkylated with Me 4-(bromomethyl)benzoate, the nitro group reduced to the amine over Pt/C, and the compound reacted with cyclopentylcarbonyl chloride to form the amide. The amide was **treated** with with Ph3PBr2 in CH2Cl2 to convert the protected alc. to the bromide and then reacted with phenethyl mercaptan in the presence of Cs2CO3 followed by NaOH to yield 4-({3-chloro-5-[(cyclopentylcarbonyl)amino]-2-[(phenethylsulfanyl)methyl]-1H-indol-1-yl}methyl)benzoic acid (III). The title compds. are useful as phospholipase enzyme inhibitors, especially cytosolic phospholipase A2 (cPLA2), for **treatment** of inflammatory conditions, particularly where inhibition of production of prostaglandins, leukotrienes, and PAF are all desired (no data).

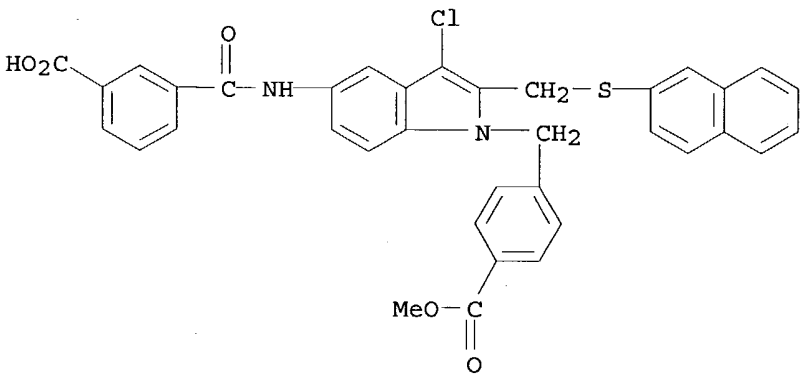
IT **241493-73-2P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of indole derivs. as phospholipase enzyme inhibitors for **treatment** of inflammatory conditions)

RN 241493-73-2 CAPLUS

CN Benzoic acid, 4-[[5-[(3-carboxybenzoyl)amino]-3-chloro-2-[(2-naphthalenylthio)methyl]-1H-indol-1-yl]methyl]-, 1-methyl ester (9CI) (CA INDEX NAME)



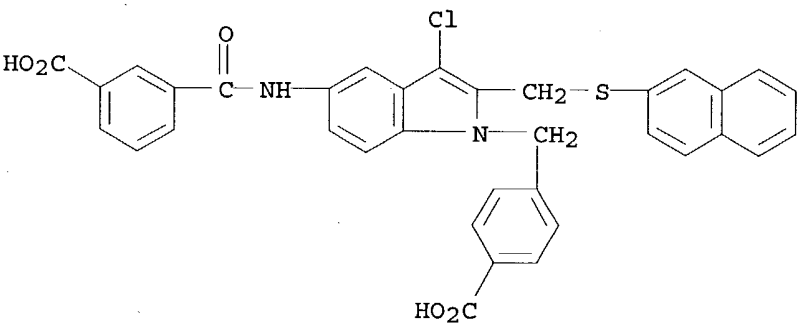
IT **241492-78-4P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of indole derivs. as phospholipase enzyme inhibitors for **treatment** of inflammatory conditions)

RN 241492-78-4 CAPLUS

CN Benzoic acid, 3-[[[1-[(4-carboxyphenyl)methyl]-3-chloro-2-[(2-naphthalenylthio)methyl]-1H-indol-5-yl]amino]carbonyl]- (9CI) (CA INDEX NAME)



L6 ANSWER 15 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:350650 CAPLUS

DOCUMENT NUMBER: 131:18925

TITLE: Preparation of cyclic amine derivatives for inhibition of the action of chemokines such as MIP-1α and/or MCP-1 on target cells

INVENTOR(S): Shiota, Tatsuki; Kataoka, Kenichiro; Imai, Minoru; Tsutsumi, Takaharu; Sudoh, Masaki; Sogawa, Ryo; Morita, Takuya; Hada, Takahiko; Muroga, Yumiko; Takenouchi, Osami; Furuya, Monoru; Endo, Noriaki; Tarby, Christine M.; Moree, Wil A.; Teig, Steven L.

PATENT ASSIGNEE(S): Teijin Ltd., Japan; Combichem, Inc.

SOURCE: PCT Int. Appl., 374 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

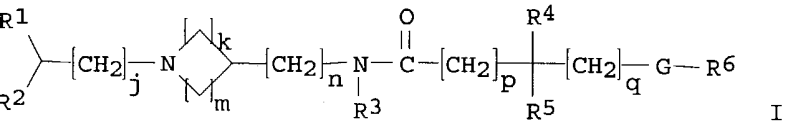
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 9925686	A1	19990527	WO 1998-US23254		19981117	<--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM						
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG						
CA 2309328	AA	19990527	CA 1998-2309328		19981117	<--
AU 9913741	A1	19990607	AU 1999-13741		19981117	<--
AU 744685	B2	20020228				
EP 1030840	A1	20000830	EP 1998-957495		19981117	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO						
TR 200001399	T2	20001121	TR 2000-200001399		19981117	<--
BR 9814645	A	20010731	BR 1998-14645		19981117	
EE 200000294	A	20010815	EE 2000-200000294		19981117	
JP 2001523661	T2	20011127	JP 2000-521070		19981117	
RU 2216540	C2	20031120	RU 2000-112403		19981117	
HR 2000000214	A1	20011231	HR 2000-214		20000413	
NO 2000002486	A	20000718	NO 2000-2486		20000512	<--
BG 104441	A	20010131	BG 2000-104441		20000516	
US 6451842	B1	20020917	US 2000-554562		20000516	
PRIORITY APPLN. INFO.:			US 1997-972484	A	19971118	
			US 1998-55285	A	19980406	
			US 1998-133434	A	19980813	
			WO 1998-US23254	W	19981117	

OTHER SOURCE(S): MARPAT 131:18925

GI



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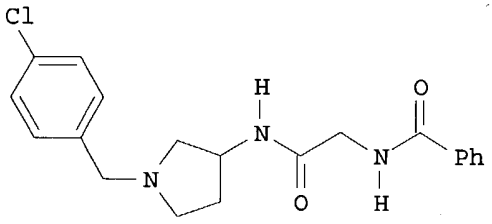


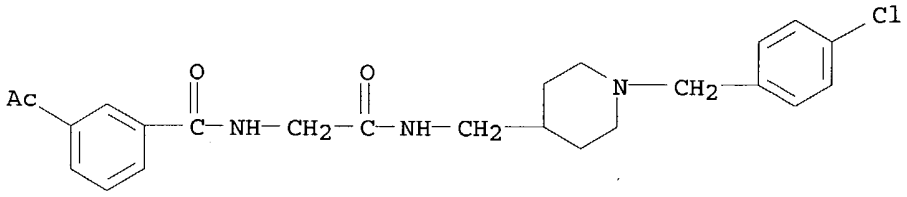
II

AB The title compds. [I; R1 = (un)substituted Ph, cycloalkyl, heteroaryl, etc.; R2 = H, alkyl, alkoxycarbonyl, etc.; j = 0-2; k = 0-2; m = 2-4; n = 0-1; R3 = H, alkyl; R4, R5 = H, OH< Ph, etc.; p = 0-1; q = 0-1; G = CO, SO, CO2, etc.; R6 = Ph, cycloalkyl, cycloalkenyl, etc.] and their pharmaceutically acceptable acid addition salts which inhibit the action of chemokines such as MIP-1α and/or MCP-1 on target cells and may be useful as a therapeutic drug and/or preventative drug in diseases, such as atherosclerosis, **rheumatoid arthritis**, and the like where blood monocytes and lymphocytes infiltrate into tissues, were prepared Thus, reaction of N-benzoylglycine with 3-amino-1-(4-chlorobenzyl)pyrrolidine.2HCl in the presence of 3-ethyl-1-[3-(dimethylaminopropyl)]carbodiimide.HCl, 1-hydroxybenzotriazole and Et3N in CHCl3 afforded 95% II which showed 50-80% inhibition of MIP-1α binding to THP-1 cells at 10 μM.

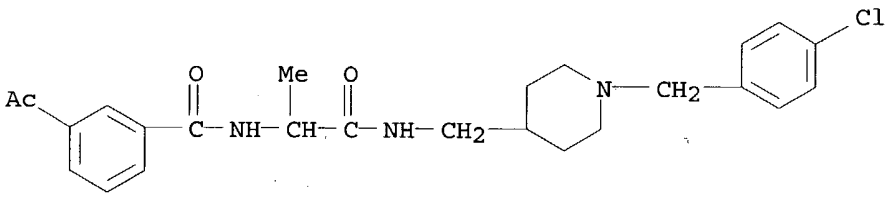
IT **226231-26-1P 226232-13-9P 226232-44-6P**

226232-66-2P 226232-70-8P 226233-28-9P
226233-64-3P 226233-91-6P 226241-34-5P
226241-35-6P 226241-39-0P 226241-41-4P
226250-69-7P 226250-73-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cyclic amine derivs. for inhibition of the action of chemokines such as MIP-1α and/or MCP-1 on target cells)

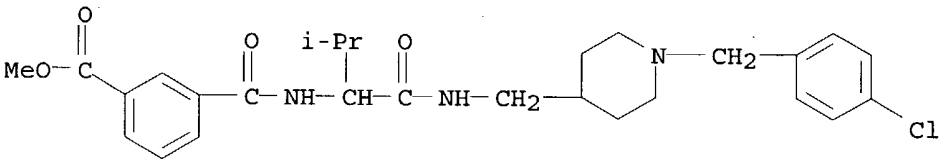
RN 226231-26-1 CAPLUS
CN Benzamide, 3-acetyl-N-[2-[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)



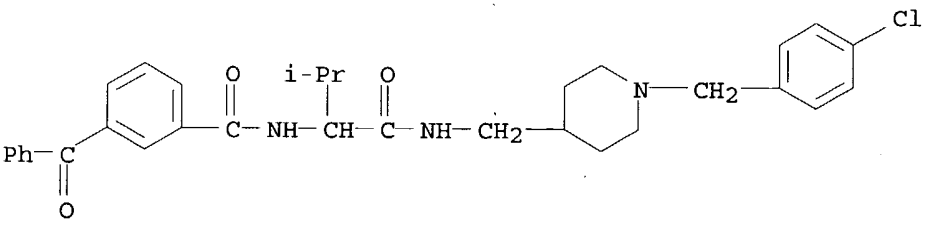
RN 226232-13-9 CAPLUS
CN Benzamide, 3-acetyl-N-[2-[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]-1-methyl-2-oxoethyl]- (9CI) (CA INDEX NAME)



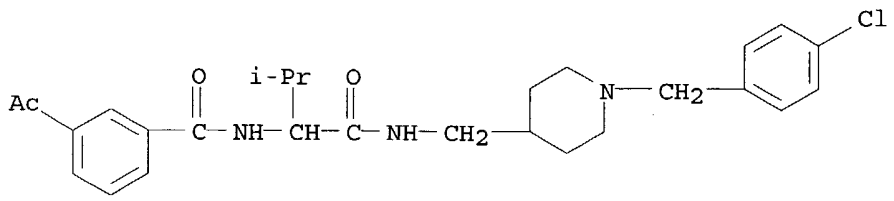
RN 226232-44-6 CAPLUS
CN Benzoic acid, 3-[[[1-[[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]carbonyl]-2-methylpropyl]amino]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



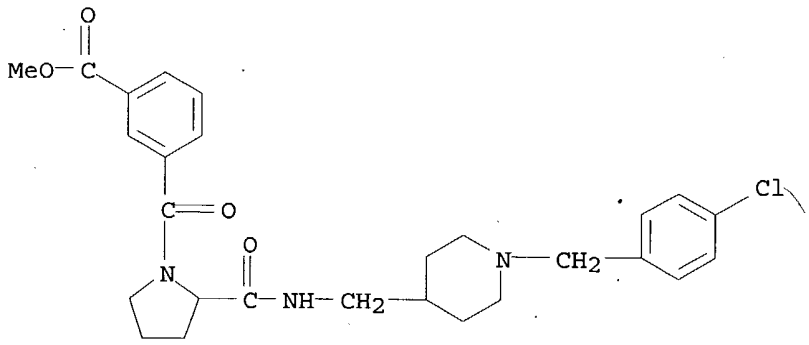
RN 226232-66-2 CAPLUS
CN Benzamide, 3-benzoyl-N-[1-[[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]carbonyl]-2-methylpropyl]- (9CI) (CA INDEX NAME)



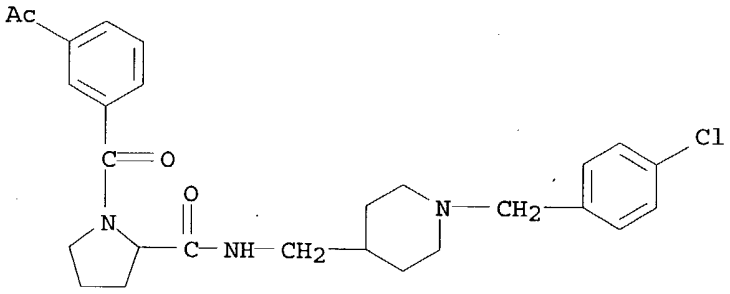
RN 226232-70-8 CAPLUS
CN Benzamide, 3-acetyl-N-[1-[[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]carbonyl]-2-methylpropyl]- (9CI) (CA INDEX NAME)



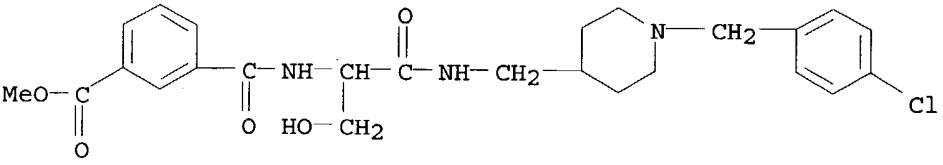
RN 226233-28-9 CAPLUS
CN Benzoic acid, 3-[[2-[[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]carbonyl]-1-pyrrolidinyl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 226233-64-3 CAPLUS
CN 2-Pyrrolidinecarboxamide, 1-(3-acetylbenzoyl)-N-[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)

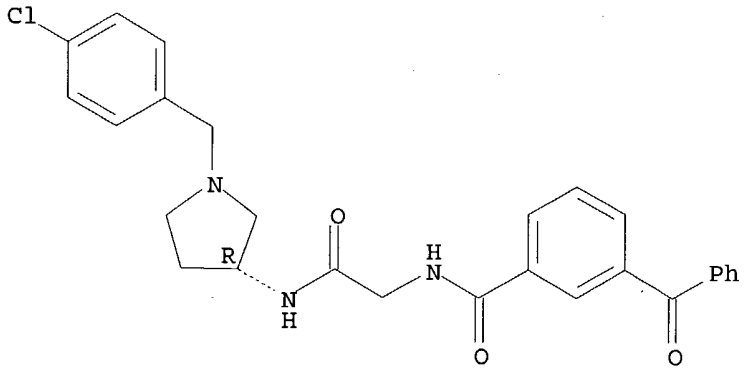


RN 226233-91-6 CAPLUS
CN Benzoic acid, 3-[[[2-[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]-1-(hydroxymethyl)-2-oxoethyl]amino]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



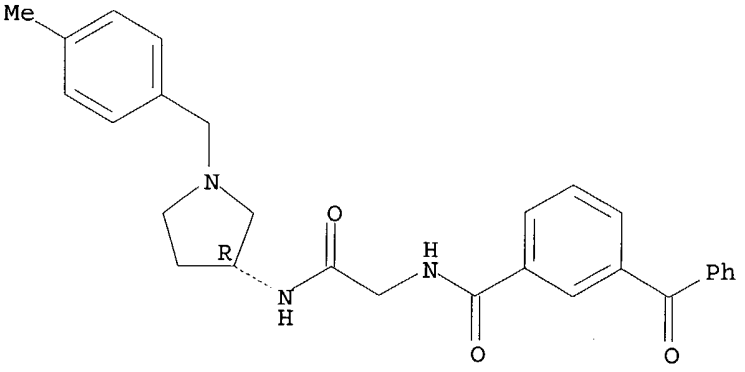
RN 226241-34-5 CAPLUS
CN Benzamide, 3-benzoyl-N-[2-[[(3R)-1-[(4-chlorophenyl)methyl]-3-pyrrolidinyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



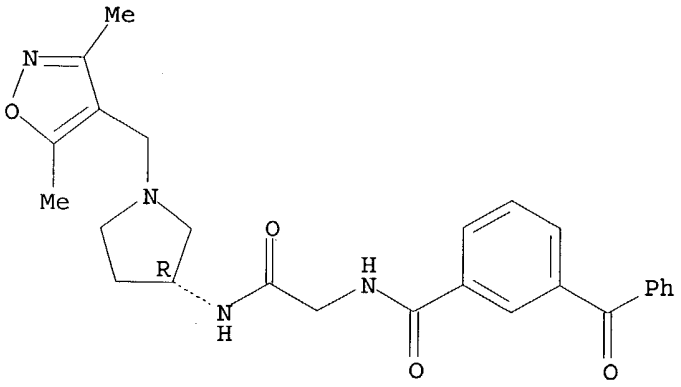
RN 226241-35-6 CAPLUS
CN Benzamide, 3-benzoyl-N-[2-[[(3R)-1-[(4-methylphenyl)methyl]-3-pyrrolidinyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

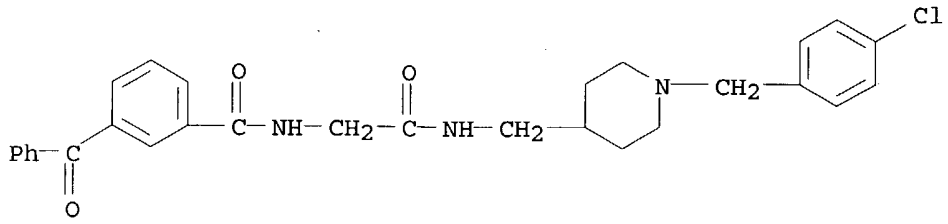


RN 226241-39-0 CAPLUS
CN Benzamide, 3-benzoyl-N-[2-[[(3R)-1-[(3,5-dimethyl-4-isoxazolyl)methyl]-3-pyrrolidinyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



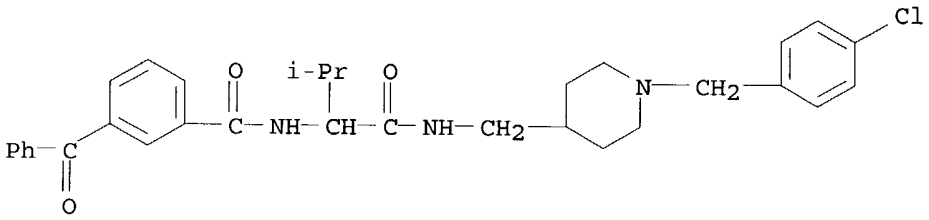
RN 226241-41-4 CAPLUS
CN Benzamide, 3-benzoyl-N-[2-[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)



RN 226250-69-7 CAPLUS
CN Benzamide, 3-benzoyl-N-[1-[[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]carbonyl]-2-methylpropyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

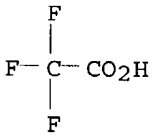
CM 1

CRN 226232-66-2
CMF C32 H36 Cl N3 O3



CM 2

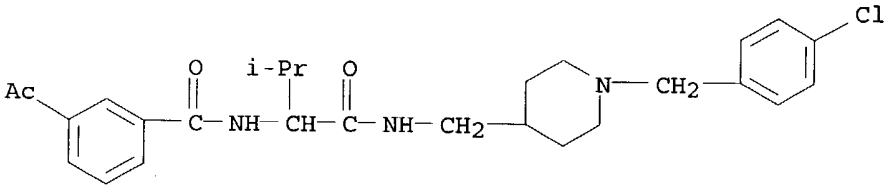
CRN 76-05-1
CMF C2 H F3 O2



RN 226250-73-3 CAPLUS
CN Benzamide, 3-acetyl-N-[1-[[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]carbonyl]-2-methylpropyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

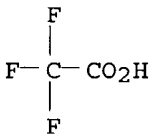
CRN 226232-70-8
CMF C27 H34 Cl N3 O3



CM 2

CRN 76-05-1

CMF C2 H F3 O2



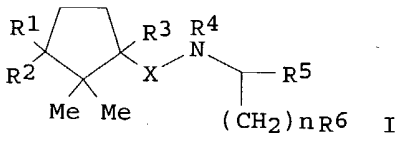
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 16 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:27805 CAPLUS
DOCUMENT NUMBER: 130:95843
TITLE: Preparation of cyclopentylcarbonylamino acid as inhibitors of α4β1 mediated cell adhesion
INVENTOR(S): Lobl, Thomas J.; Rishton, Gil; Teegarden, Bradley; Polinsky, Alex; Yamagishi, Masafumi; Tanis, Steven P.; Fisher, Jed F.; Thomas, Edward W.; Chrusciel, Robert A.
PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Japan; Pharmacia & Upjohn Company
SOURCE: PCT Int. Appl., 342 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9858902	A1	19981230	WO 1998-US13064	19980623 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9881633	A1	19990104	AU 1998-81633	19980623 <--
EP 991619	A1	20000412	EP 1998-931521	19980623 <--
EP 991619	B1	20030910		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001517246	T2	20011002	JP 1999-504997	19980623
US 6482849	B1	20021119	US 1998-102584	19980623
AT 249421	E	20030915	AT 1998-931521	19980623
PT 991619	T	20040227	PT 1998-931521	19980623
ES 2206953	T3	20040516	ES 1998-931521	19980623
US 2003130349	A1	20030710	US 2002-193137	20020712
US 6596752	B1	20030722		

PRIORITY APPLN. INFO.:
US 1997-50515P P 19970623
US 1998-102584 A3 19980623
WO 1998-US13064 W 19980623

OTHER SOURCE(S): MARPAT 130:95843
GI



I

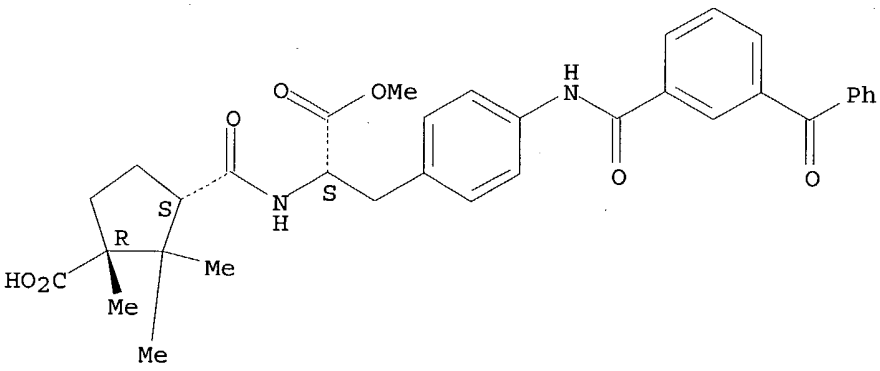
AB Title compds. [I; n = 0, 1; R1 = H, CH3; R2 = CN, CO2H, CONH2, CONHOCH2Ph, NHCOOCH2Ph, etc.; R3 = H, CH3; X = CH, CO; R4 = H, alkyl; R5 = CO2H, CONH2, COOR, etc.; R = alkyl; R6 = aryl, heteroaryl, arylcarbonyl, aarylcarbonylaminoalkyl, etc.], a pharmaceutically acceptable salt, a stereoisomer thereof are prepared as inhibitors of α4β1 mediated adhesion to either VCAM or CS-1 and which can be used for **treating** or preventing α4β1 adhesion mediated conditions in human such as inflammatory diseases. Thus, (1S-cis)- N-[(3-carboxy-2,2,3-trimethylcyclopentyl)carbonyl]-O-(phenylmethyl)-L-tyrosine was prepared and assayed for inhibition of β1-mediated cell adhesion in vitro.

IT **219494-75-4P 219494-76-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cyclopentylcarbonylamino acid as inhibitors of α4β1 mediated cell adhesion)

RN 219494-75-4 CAPLUS

CN L-Phenylalanine, 4-[(3-benzoylbenzoyl)amino]-N-[[(1S,3R)-3-carboxy-2,2,3-trimethylcyclopentyl]carbonyl]-, α-methyl ester (9CI) (CA INDEX NAME)

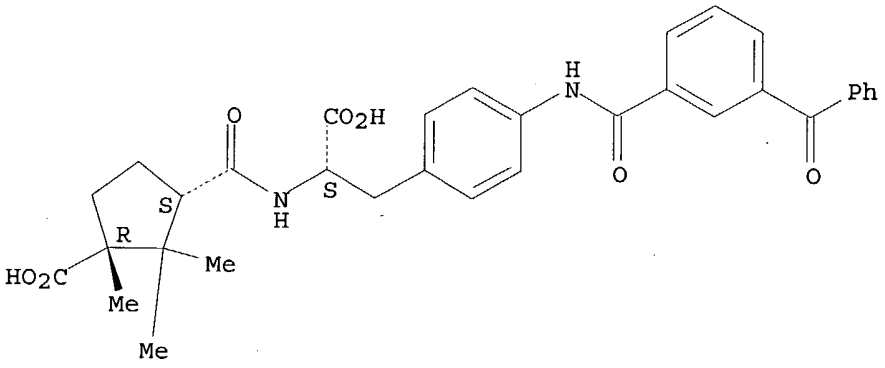
Absolute stereochemistry.



RN 219494-76-5 CAPLUS

CN L-Phenylalanine, 4-[(3-benzoylbenzoyl)amino]-N-[[(1S,3R)-3-carboxy-2,2,3-trimethylcyclopentyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 17 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:693417 CAPLUS

DOCUMENT NUMBER: 129:343326

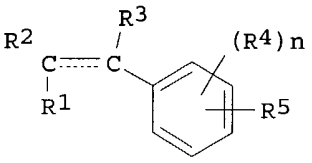
TITLE: Preparation of benzenes as protein kinase C inhibitors

INVENTOR(S): Mori, Toyoki; Tominaga, Michiaki; Tabusa, Fujio; Ei, Kazuyoshi; Nakaya, Kenji; Takemura, Isao; Shinohara, Tomokazu; Tanada, Yoshihisa; Yamauchi, Takahito;

	Kitano, Kazuyoshi
PATENT ASSIGNEE(S):	Otsuka Pharmaceutical Co., Ltd., Japan
SOURCE:	Jpn. Kokai Tokkyo Koho, 359 pp.
	CODEN: JKXXAF
DOCUMENT TYPE:	Patent
LANGUAGE:	Japanese
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 10287634	A2	19981027	JP 1997-110527	19970411 <--
PRIORITY APPLN. INFO.:			JP 1997-110527	19970411
OTHER SOURCE(S):	MARPAT 129:343326			

GI



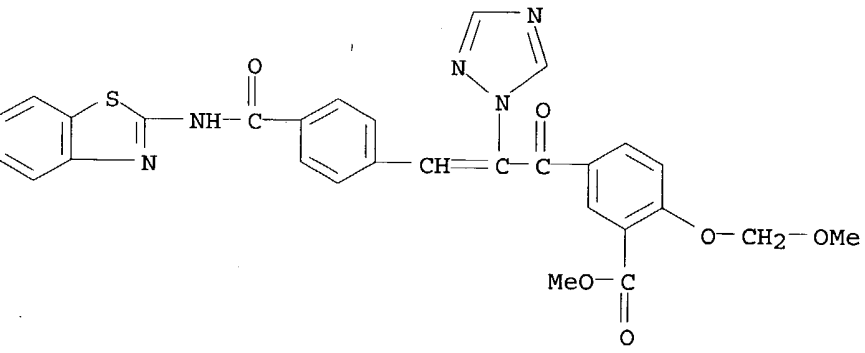
I

AB Benzenes I [R1 = 5- to 6-membered (un)substituted unsatd. heterocyclyl having 1-4 N, O, or S; cyano, carboxylalkyl, alkoxycarbonyl, H, Bz, (un)substituted amido, etc.; R2 = (un)substituted Bz, (un)substituted 1,2,3,4-tetrahydroquinolinylcarbonyl, pyridylcarbonyl, (un)substituted phenoxycarbonyl, etc.; R3 = H, lower alkyl, PhS, (un)substituted lower alkylthio, cycloalkylthio, cyano, etc.; R4 = H, (un)substituted lower alkyl, lower alkoxy, (un)substituted aminoalkylene, (un)substituted aminoalkylenyloxy; R5 = substituted alkenyl, phenylthioureidocarbonyl, pyrimidylaminocarbonylalkoxy, etc.; n = 1-3; the dot line may be double bond] or their salts are prepared I are useful for prevention and **treatment** of chronic **rheumatoid arthritis**, systemic lupus erythematosus, atopic dermatitis, **heart failure**, allergy, multiple sclerosis, tumor, Alzheimer-type dementia, etc. Condensation of 250 mg 2-(benzoylmethyl)pyridine with 300 mg 4-[(2-benzothiazolyl)aminocarbonyl]benzaldehyde in C6H6 for 10 h gave 0.3 g 2-[4-[2-benzoyl-2-(2-pyridyl)vinyl]benzoylamino]benzothiazole.

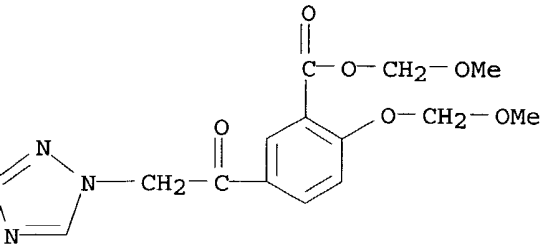
IT **215504-19-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of benzenes as protein kinase C inhibitors for **treatment** of diseases)

RN 215504-19-1 CAPLUS

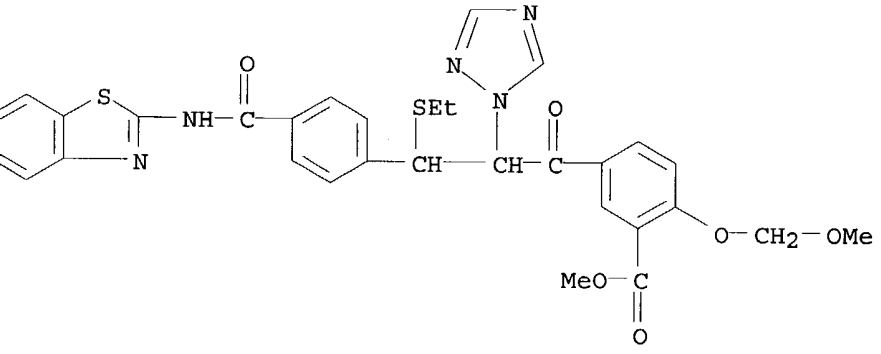
CN Benzoic acid, 5-[3-[4-[(2-benzothiazolylamino)carbonyl]phenyl]-1-oxo-2-(1H-1,2,4-triazol-1-yl)-2-propenyl]-2-(methoxymethoxy)-, methyl ester (9CI) (CA INDEX NAME)



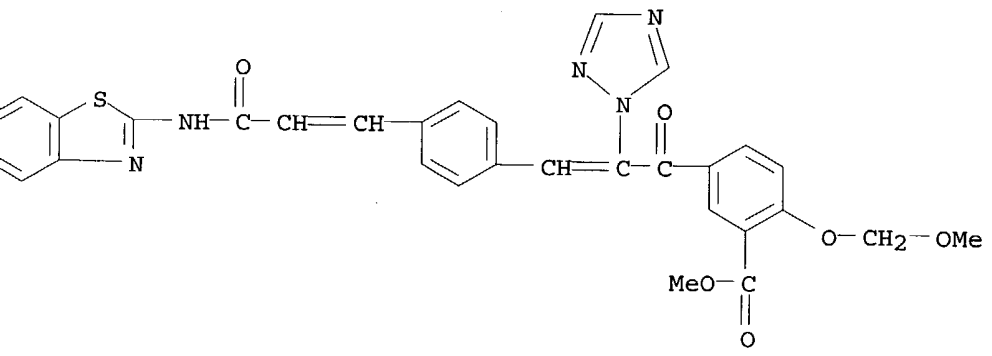
IT **215503-79-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of benzenes as protein kinase C inhibitors for **treatment** of diseases)
RN 215503-79-0 CAPLUS
CN Benzoic acid, 2-(methoxymethoxy)-5-(1H-1,2,4-triazol-1-ylacetyl)-, methoxymethyl ester (9CI) (CA INDEX NAME)



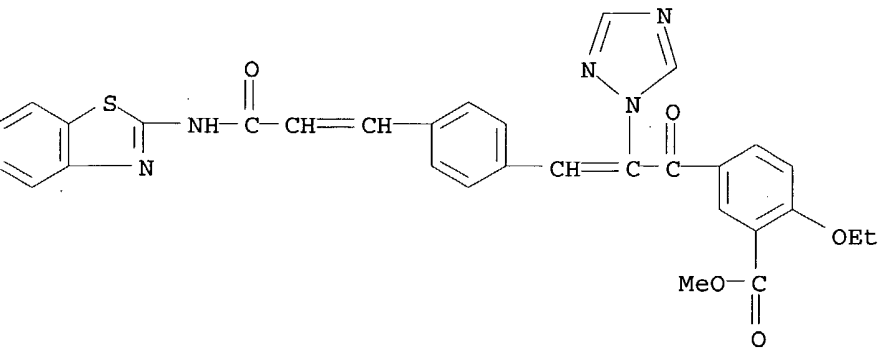
IT **215504-20-4P 215504-43-1P 215504-55-5P**
215504-56-6P 215504-69-1P 215504-93-1P
215504-94-2P 215504-96-4P 215505-17-2P
215505-94-5P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzenes as protein kinase C inhibitors for **treatment** of diseases)
RN 215504-20-4 CAPLUS
CN Benzoic acid, 5-[3-[4-[(2-benzothiazolylamino)carbonyl]phenyl]-3-(ethylthio)-1-oxo-2-(1H-1,2,4-triazol-1-yl)propyl]-2-(methoxymethoxy)-, methyl ester (9CI) (CA INDEX NAME)



RN 215504-43-1 CAPLUS
CN Benzoic acid, 5-[3-[4-[3-(2-benzothiazolylamino)-3-oxo-1-propenyl]phenyl]-1-oxo-2-(1H-1,2,4-triazol-1-yl)-2-propenyl]-2-(methoxymethoxy)-, methyl ester (9CI) (CA INDEX NAME)

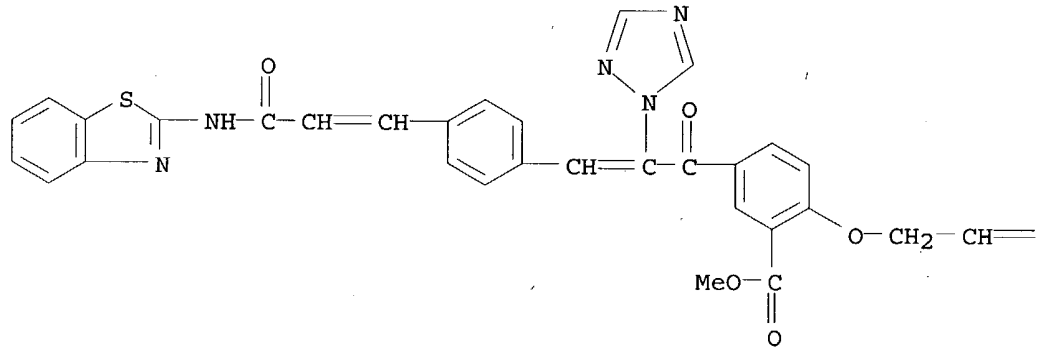


RN 215504-55-5 CAPLUS
CN Benzoic acid, 5-[3-[4-[3-(2-benzothiazolylamino)-3-oxo-1-propenyl]phenyl]-1-oxo-2-(1H-1,2,4-triazol-1-yl)-2-propenyl]-2-ethoxy-, methyl ester (9CI) (CA INDEX NAME)



RN 215504-56-6 CAPLUS
CN Benzoic acid, 5-[3-[4-[3-(2-benzothiazolylamino)-3-oxo-1-propenyl]phenyl]-1-oxo-2-(1H-1,2,4-triazol-1-yl)-2-propenyl]-2-(2-propenyloxy)-, methyl ester (9CI) (CA INDEX NAME)

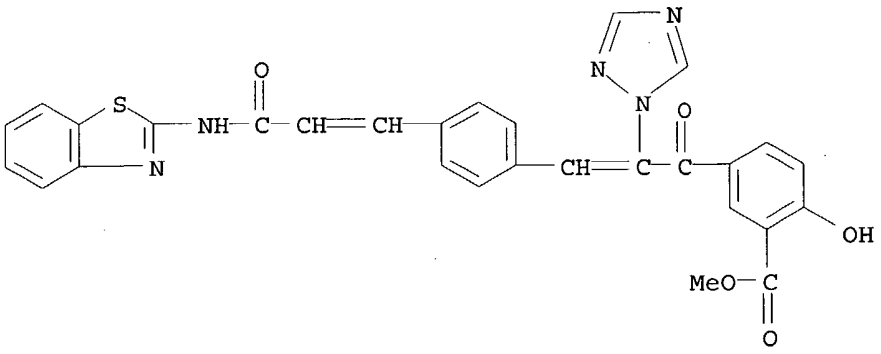
PAGE 1-A



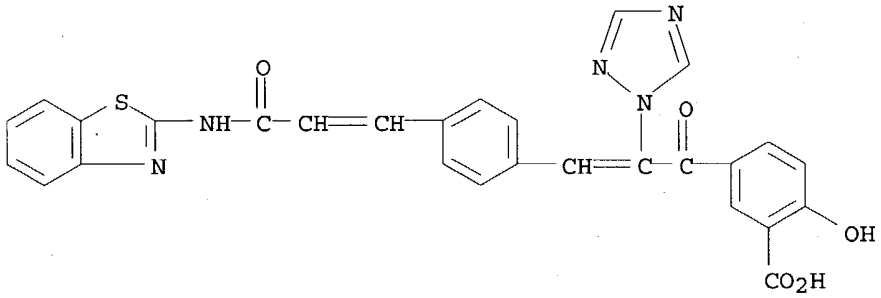
PAGE 1-B

$=CH_2$

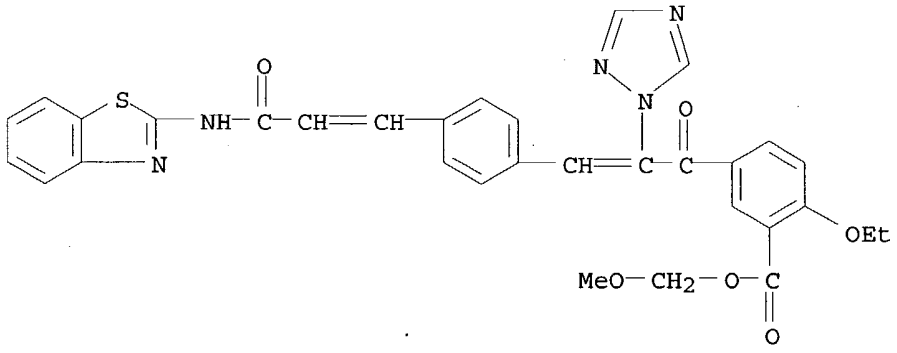
RN 215504-69-1 CAPLUS
CN Benzoic acid, 5-[3-[4-[3-(2-benzothiazolylamino)-3-oxo-1-propenyl]phenyl]-1-oxo-2-(1H-1,2,4-triazol-1-yl)-2-propenyl]-2-hydroxy-, methyl ester (9CI) (CA INDEX NAME)



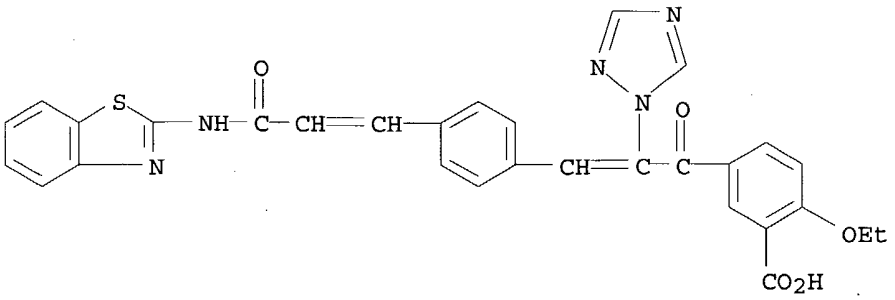
RN 215504-93-1 CAPLUS
CN Benzoic acid, 5-[3-[4-[3-(2-benzothiazolylamino)-3-oxo-1-propenyl]phenyl]-1-oxo-2-(1H-1,2,4-triazol-1-yl)-2-propenyl]-2-hydroxy- (9CI) (CA INDEX NAME)



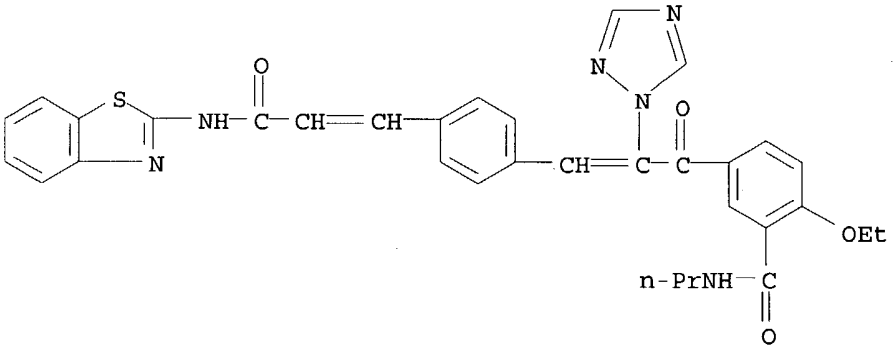
RN 215504-94-2 CAPLUS
CN Benzoic acid, 5-[3-[4-[3-(2-benzothiazolylamino)-3-oxo-1-propenyl]phenyl]-1-oxo-2-(1H-1,2,4-triazol-1-yl)-2-propenyl]-2-ethoxy-, methoxymethyl ester (9CI) (CA INDEX NAME)



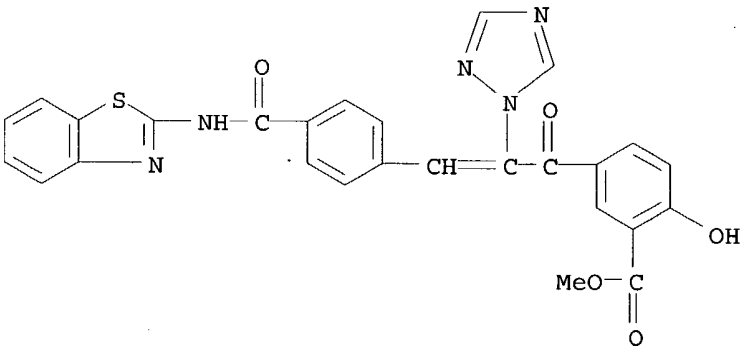
RN 215504-96-4 CAPLUS
CN Benzoic acid, 5-[3-[4-[3-(2-benzothiazolylamino)-3-oxo-1-propenyl]phenyl]-1-oxo-2-(1H-1,2,4-triazol-1-yl)-2-propenyl]-2-ethoxy- (9CI) (CA INDEX NAME)



RN 215505-17-2 CAPLUS
CN Benzamide, 5-[3-[4-[3-(2-benzothiazolylamino)-3-oxo-1-propenyl]phenyl]-1-oxo-2-(1H-1,2,4-triazol-1-yl)-2-propenyl]-2-ethoxy-N-propyl- (9CI) (CA INDEX NAME)



RN 215505-94-5 CAPLUS
CN Benzoic acid, 5-[3-[4-[(2-benzothiazolylamino)carbonyl]phenyl]-1-oxo-2-(1H-1,2,4-triazol-1-yl)-2-propenyl]-2-hydroxy-, methyl ester (9CI) (CA INDEX NAME)



L6 ANSWER 18 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:682372 CAPLUS
DOCUMENT NUMBER: 129:316232
TITLE: Preparation of compounds and compositions for **treating** diseases associated with serine protease, particularly tryptase, activity
INVENTOR(S): Church, Timothy J.; Cutshall, Neil Scott; Gangloff, Anthony R.; Jenkins, Thomas E.; Linsell, Martin S.; Litvak, Joane; Rice, Kenneth D.; Spencer, Jeffrey R.; Wang, Vivian R.
PATENT ASSIGNEE(S): Axys Pharmaceuticals Corporation, USA
SOURCE: PCT Int. Appl., 108 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9845275	A1	19981015	WO 1997-US21849	19971201 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9858950	A1	19981030	AU 1998-58950	19971201 <--
AU 752064	B2	20020905		
CN 1251579	A	20000426	CN 1997-182098	19971201 <--
EE 9900477	A	20000615	EE 1999-477	19971201 <--
EE 4055	B1	20030616		
EP 1019382	A1	20000719	EP 1997-954520	19971201 <--
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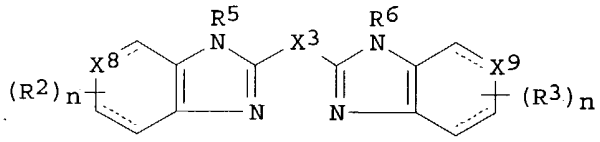
NZ 500029	A	20010223	NZ 1997-500029	19971201
JP 2001519806	T2	20011023	JP 1998-542739	19971201
MX 9909006	A	20000831	MX 1999-9006	19991001 <--
NO 9904858	A	19991206	NO 1999-4858	19991006 <--
LV 12495	B	20010120	LV 1999-153	19991102
LT 4704	B	20000925	LT 1999-131	19991105 <--
US 2001053779	A1	20011220	US 2001-874412	20010604
US 6562854	B2	20030513		
US 2003212120	A1	20031113	US 2003-401415	20030314

PRIORITY APPLN. INFO.:		
US 1997-833674	A	19970407
US 1994-357491	B2	19941214
US 1997-980515	A1	19971201
WO 1997-US21849	W	19971201
US 2001-874412	A1	20010604

OTHER SOURCE(S): CASREACT 129:316232; MARPAT 129:316232
GI



I

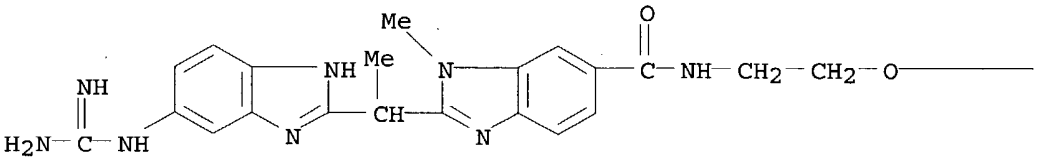
AB A preferred aspect of the invention are compds. of Formula [I; in which: the dashed lines independently represent optional bonds; each R2 independently is (C1-6)alkyl, (C1-6)alkyloxy, halo or hydroxy; each R3 independently is (C1-6)alkyl, (C1-6)alkyloxy, halo or hydroxy; X3 is -C(O)- or -CR7R8-, X8 is -CH(R1)n1- or -C(R1)n1=, wherein R1 is amino(N1-4)azolidinyl, amino(N1-4)azolyl, (N1-4)azolidinyl, (N1-4)azolyl, etc.; X8 is -N= or -NH(R1)n1-, wherein R1 is -C(NR9)R9, -C(NH)NHR10 or -C(NH)NR10R10, wherein R9 independently is hydrogen or (C1-6)alkyl and each R10 independently is (C1-6)alkyl; and X9 is -CH(R4)- or -C(R4)=, wherein R4 is -R12, -OR12, -N(R13)R12, etc.; wherein R4 is -C(O)R12, -C(O)OR12, -C(O)N(R13)R12, etc.; R12 is cyano, guanidino, halo, alkyl, etc.; R13 is hydrogen, alkyl; R5 is hydrogen or (C1-4)alkyl, R6 is hydrogen or (C1-4) alkyl; R7 is hydrogen, methyl; R8 is hydrogen Me, hydroxy; n = 0-4]. The compds., compns. and methods are effective for the prevention and **treatment** of inflammatory diseases associated with the respiratory tract, such as asthma and allergic rhinitis, as well as other types of immunomediated inflammatory disorders, such as **rheumatoid arthritis**, conjunctivitis and inflammatory bowel disease, various dermatol. conditions, as well as certain viral

conditions. The compds. comprise potent and selective inhibitors of the mast-cell protease tryptase. The compns. for **treating** these conditions include oral, inhalant, topical and parenteral prepns. as well as devices comprising such prepns.

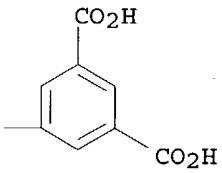
IT **214781-30-3P 214781-74-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of arenoimidazoles for **treating** human inflammatory disorder)

RN 214781-30-3 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-[2-[[[2-[1-[5-[(aminoiminomethyl)amino]-1H-benzimidazol-2-yl]ethyl]-1-methyl-1H-benzimidazol-6-yl]carbonyl]amino]ethoxy]- (9CI) (CA INDEX NAME)

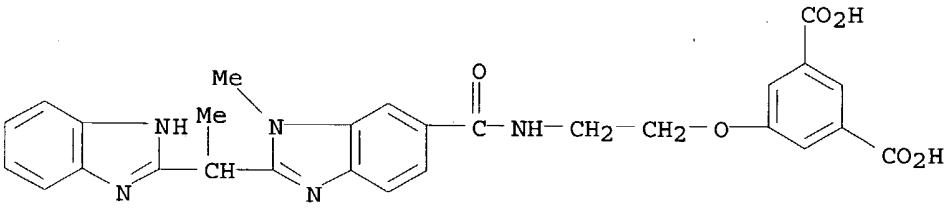
PAGE 1-A



PAGE 1-B



RN 214781-74-5 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-[2-[[[2-[1-(1H-benzimidazol-2-yl)ethyl]-1-methyl-1H-benzimidazol-6-yl]carbonyl]amino]ethoxy]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

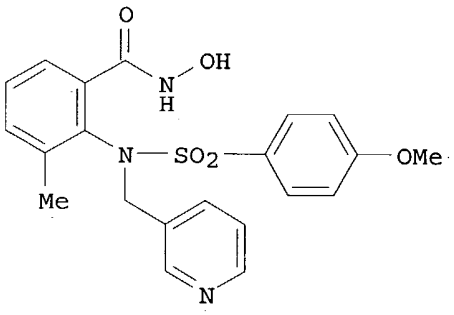
L6 ANSWER 19 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:251153 CAPLUS
DOCUMENT NUMBER: 128:308308
TITLE: The preparation and use of ortho-sulfonamido aryl hydroxamic acids as matrix metalloproteinase and TACE inhibitors
INVENTOR(S): Levin, Jeremy Ian; Du Mila, T.; Venkatesan, Aranapakam Mudumbai; Nelson, Frances Christy; Zask, Arie; Gu, Yansong
PATENT ASSIGNEE(S): American Cyanamid Company, USA
SOURCE: PCT Int. Appl., 164 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9816503	A2	19980423	WO 1997-US18280	19971008 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2268894	AA	19980423	CA 1997-2268894	19971008 <--
AU 9851458	A1	19980511	AU 1998-51458	19971008 <--
AU 731737	B2	20010405		
EP 938471	A1	19990901	EP 1997-946246	19971008 <--
EP 938471	B1	20011212		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
BR 9712525	A	19991019	BR 1997-12525	19971008 <--
CN 1240429	A	20000105	CN 1997-180613	19971008 <--
JP 2001504809	T2	20010410	JP 1998-518448	19971008
AT 210637	E	20011215	AT 1997-946246	19971008
ES 2166102	T3	20020401	ES 1997-946246	19971008
PT 938471	T	20020531	PT 1997-946246	19971008
ZA 9709233	A	19990415	ZA 1997-9233	19971015 <--
TW 410220	B	20001101	TW 1997-86114187	19971015 <--
KR 2000049196	A	20000725	KR 1999-703294	19990415 <--
HK 1021178	A1	20020404	HK 2000-100090	20000106

PRIORITY APPLN. INFO.: US 1996-732631 A 19961016
WO 1997-US18280 W 19971008

OTHER SOURCE(S): MARPAT 128:308308
GI



II

AB The invention relates to novel, low mol. weight, non-peptide inhibitors of matrix metalloproteinases (e.g. gelatinases, stromelysins and collagenases) and TNF-α converting enzyme (TACE, tumor necrosis factor-α converting enzyme). The compds. are useful for the **treatment** of diseases in which these enzymes are implicated such as arthritis, tumor growth and metastasis, angiogenesis, tissue ulceration, abnormal wound healing, periodontal disease, bone disease, proteinuria, aneurysmal aortic disease, degenerative cartilage loss following traumatic joint injury, demyelinating diseases of the nervous system, graft rejection, cachexia, anorexia, inflammation, fever, insulin resistance, septic shock, congestive **heart failure**, inflammatory disease of the central nervous system, inflammatory bowel disease, HIV infection, age related macular degeneration, diabetic retinopathy, proliferative vitreoretinopathy, retinopathy of prematurity, ocular inflammation, keratoconus, Sjogren's syndrome, myopia, ocular tumors, and ocular angiogenesis/neovascularization. The invention compds. are represented by the formula ZSO2N(CH2R7)ACONHOH [I; A = (un)substituted

Ph or naphthyl; Z = (un)substituted aryl, heteroaryl, or benzo-fused heteroaryl; R7 = H, (un)substituted alk(en/yn)yl, Ph, naphthyl, 5- or 6-membered heteroaryl, cycloalkyl, or cycloheteroalkyl; or R7CH2NA forms a non-aromatic 1,2-benzo-fused 7- to 10-membered heterocyclic ring with an optional addition benzo fusion; where the hydroxamic acid moiety and the sulfonamido moiety are bonded to adjacent carbons on group A], and include pharmaceutically acceptable salts, optical isomers, and diastereomers. Prepns. of over 400 compds., including I and their intermediates, are given. For instance, 2-[(4-methoxybenzenesulfonyl)amino]-3-methylbenzoic acid Me ester (preparation given) was N-alkylated by 3-picolyl chloride-HCl (83%), followed by hydrolysis of the ester with LiOH in aqueous THF (100%), activation with oxalyl chloride, and hydroxamidation with NH2OH.HCl (51%), to give title compound II. At 50 mg/kg/day in rats with cartilage implants, II gave 44.6% inhibition of cartilage weight loss, and 51.2% inhibition of cartilage collagen loss.

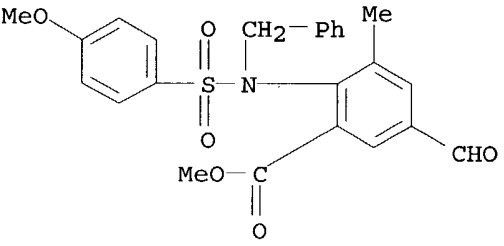
IT **206549-41-9P 206549-42-0P 206549-43-1P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of ortho-sulfonamido aryl hydroxamic acids as matrix metalloproteinase and TACE inhibitors)

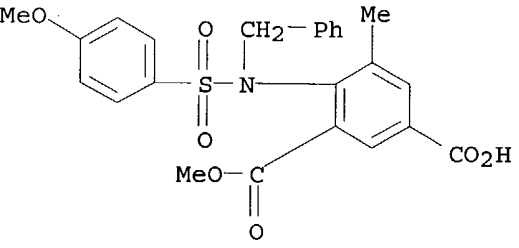
RN 206549-41-9 CAPLUS

CN Benzoic acid, 5-formyl-2-[[(4-methoxyphenyl)sulfonyl](phenylmethyl)amino]-3-methyl-, methyl ester (9CI) (CA INDEX NAME)



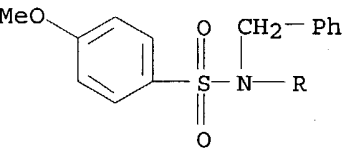
RN 206549-42-0 CAPLUS

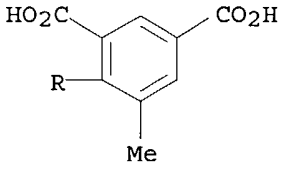
CN 1,3-Benzenedicarboxylic acid, 4-[[(4-methoxyphenyl)sulfonyl](phenylmethyl)amino]-5-methyl-, 3-methyl ester (9CI) (CA INDEX NAME)



RN 206549-43-1 CAPLUS

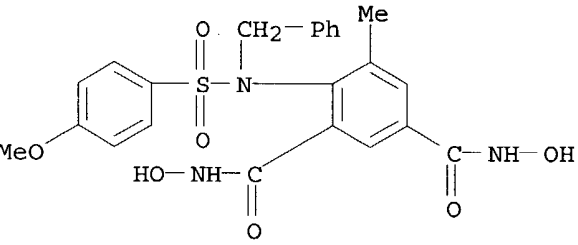
CN 1,3-Benzenedicarboxylic acid, 4-[[(4-methoxyphenyl)sulfonyl](phenylmethyl)amino]-5-methyl- (9CI) (CA INDEX NAME)



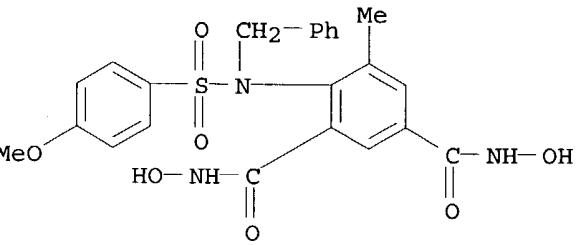


IT **206549-44-2P 206549-45-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of ortho-sulfonamido aryl hydroxamic acids as matrix metalloproteinase and TACE inhibitors)

RN 206549-44-2 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-dihydroxy-4-[[(4-methoxyphenyl)sulfonyl](phenylmethyl)amino]-5-methyl- (9CI) (CA INDEX NAME)



RN 206549-45-3 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-dihydroxy-4-[[(4-methoxyphenyl)sulfonyl](phenylmethyl)amino]-5-methyl-, disodium salt (9CI) (CA INDEX NAME)



●2 Na

L6 ANSWER 20 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:310799 CAPLUS
DOCUMENT NUMBER: 126:293363
TITLE: Preparation of 2-phenylsulfonyl- and 2-(heterocyclylsulfonyl)quinazoline derivatives as chymase inhibitors
INVENTOR(S): Fukami, Harukazu; Ito, Akiko; Niwata, Shinjiro; Kakutani, Saki; Sumida, Motoo; Kiso, Yoshinobu

PATENT ASSIGNEE(S): Suntory Limited, Japan; Fukami, Harukazu; Ito, Akiko; Niwata, Shinjiro; Kakutani, Saki; Sumida, Motoo; Kiso, Yoshinobu

SOURCE: PCT Int. Appl., 120 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

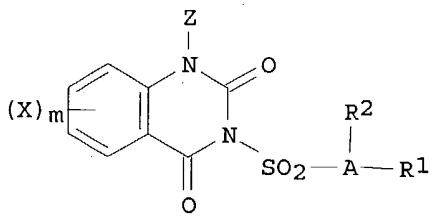
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9711941	A1	19970403	WO 1996-JP2830	19960927 <--
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 795548	A1	19970917	EP 1996-932039	19960927 <--
EP 795548	B1	20020703		
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
ES 2175127	T3	20021116	ES 1996-932039	19960927
US 5814631	A	19980929	US 1997-849114	19970528 <--

PRIORITY APPLN. INFO.:

JP 1995-285437	A	19950928
JP 1996-116557	A	19960510
WO 1996-JP2830	W	19960927

OTHER SOURCE(S): MARPAT 126:293363

GI



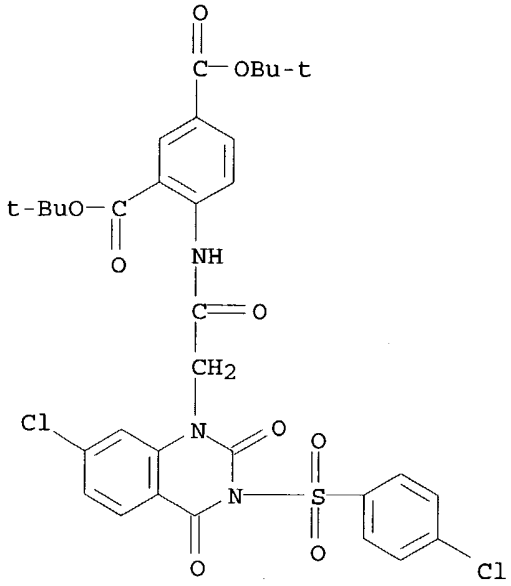
I

AB Quinazoline derivs. represented by general formula [I; group A = benzene, pyridine, pyrrole, or pyrazole ring; m = 0-2; X = OH, NO2, halo, C1-4 (halo)alkyl, or (halo)alkoxy, C7-12 aralkyloxy; X = group to form a naphthalene or quinoline ring together with the benzene ring to which X is attached; R1, R2 = H, halo, C1-4 (halo)alkyl, NO2, cyano, pyrazolyl, tetrazolyl, C1-4 alkyl, CO2H, allyloxycarbonyl, C1-4 (un)substituted alkoxy; or R1 and R2 together with the benzene ring represent a naphthalene or quinoline ring; Z = H, C1-4 (halo)alkyl, C2-5 alkenyl, (un)substituted aralkyl, aromatic heterocyclylalkyl, C1-4 alkoxycarbonylmethyl, allyloxycarbonylmethyl, (1° or 2° amino)carbonylmethyl, (un)substituted aralkyloxymethyl; proviso given] or pharmacol. acceptable salts thereof are prepared They are useful as preventives/remedies for cardiac and circulatory diseases (e.g. hypertension or **heart failure**) caused by abnormal overprodn. of angiotensin II. Thus, a quinazolinedione derivative (II; R = H) (preparation given) was condensed with 3-(diethylamino)-1,5-dihydro-2,4,3-benzodioxaphosphepine in the presence of tetrazole in DMF, followed by oxidation with m-chloroperbenzoic acid in CH2Cl2 and hydrogenolysis over 10% Pd-C in dioxane under H atmospheric to give II [R = P(O)(OH)2]. II (R = H) and II [R = P(O)(OH)2] showed IC50 of 0.060 and 0.025 μM, resp., for inhibiting human heart chymase. The title compds. I also inhibited cathepsin G and chymotrypsin. Formulation examples containing I were given.

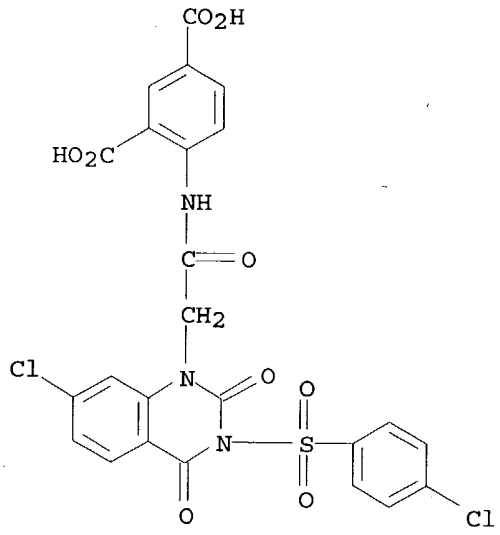
IT **189062-20-2P 189062-21-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-phenylsulfonyl- and N-(heterocyclylsulfonyl)quinazoline derivs. as chymase inhibitors for **treating** heart or circulatory diseases)

RN 189062-20-2 CAPLUS

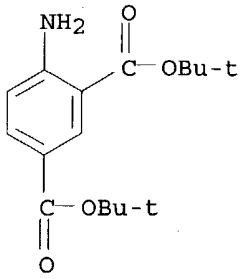
CN 1,3-Benzenedicarboxylic acid, 4-[[[7-chloro-3-[(4-chlorophenyl)sulfonyl]-3,4-dihydro-2,4-dioxo-1(2H)-quinazolinyl]acetyl]amino]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



RN 189062-21-3 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 4-[[[7-chloro-3-[(4-chlorophenyl)sulfonyl]-3,4-dihydro-2,4-dioxo-1(2H)-quinazolinyl]acetyl]amino]- (9CI) (CA INDEX NAME)



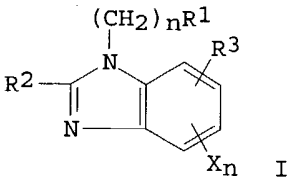
IT **189062-98-4**, 2,4-Di-tert-butoxycarbonylaniline
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of N-phenylsulfonyl- and N-(heterocyclylsulfonyl)quinazoline derivs. as chymase inhibitors for **treating** heart or circulatory diseases)
RN 189062-98-4 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 4-amino-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



L6 ANSWER 21 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:483335 CAPLUS
DOCUMENT NUMBER: 121:83335
TITLE: Preparation of substituted benzimidazoles useful as angiotensin II receptor antagonists
INVENTOR(S): Franz, Robert G.; Weinstock, Joseph
PATENT ASSIGNEE(S): SmithKline Beecham Corp., USA
SOURCE: U.S., 19 pp. Cont.-in-part of U.S. Ser No. 509,268, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5294631	A	19940315	US 1992-937885	19921013 <--
WO 9116313	A1	19911031	WO 1991-US2396	19910408 <--
W: AU, CA, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				

PRIORITY APPLN. INFO.: US 1990-509268 19900413
WO 1991-US2396 19910408
OTHER SOURCE(S): MARPAT 121:83335
GI

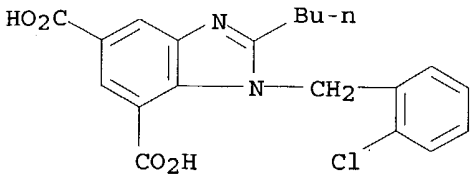


I

AB The preparation of title compds. I [R1 = CONHCH(Y)(CH2)naryl, CONHCH(Y)(CH2)nheteroaryl, substituted Ph, etc.; R2 = H, C2-10 alkyl, C3-10 alkenyl, C3-6 cycloalkyl, etc.; R3 = (CH2)nY, CH:CY(CH2)naryl, CH:CY(CH2)nheteroaryl, (CH2)nCONHCHY(CH2)naryl, etc.; Y = substituted carboxy, tetrazol-5-yl; X = halo, perfluoroalkyl, C1-6 alkyl, etc.; n = 0-2], useful in regulating hypertension and in the **treatment** of congestive **heart failure**, renal failure, and glaucoma, pharmaceutical compns. including these antagonists, and methods of using these compds. to produce angiotensin II receptor antagonism in mammals, is described. Thus, cyclization of 5-bromo-2-[(2-chlorophenyl)methyl-N-valeryl]amino-3-nitrobenzoic acid (preparation given) in the presence of sodium bicarbonate solution containing sodium hydrosulfite at Ph 7.1 followed by acidic workup gave title compound, 5-bromo-2-butyl-1-(2-chlorophenyl)methyl-1H-benzimidazole-7-carboxylic acid. The pharmaceutical compns. of some of the compds. prepared is given.

IT **138993-09-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses).

(preparation of, as angiotensin II receptor antagonist)
RN 138993-09-6 CAPLUS
CN 1H-Benzimidazole-5,7-dicarboxylic acid, 2-butyl-1-[(2-chlorophenyl)methyl]- (9CI) (CA INDEX NAME)

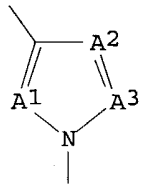
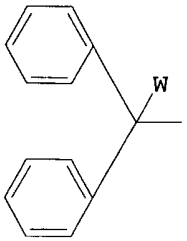
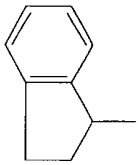


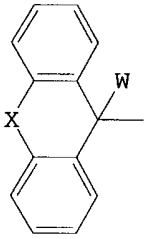
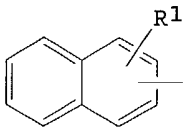
L6 ANSWER 22 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1991:656180 CAPLUS
DOCUMENT NUMBER: 115:256180
TITLE: Preparation of α-hexyl-4-(benzoylamino)-1H-imidazole-1-acetic acid, its derivatives, and analogs as angiotensin II antagonists
INVENTOR(S): Lifer, Sherryl L.; Marshall, Winston S.; Mohamadi, Fariborz; Reel, Jon K.; Simon, Richard L.; Steinberg, Mitchell I.; Whitesitt, Celia A.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Can. Pat. Appl., 79 pp.
CODEN: CPXXEB
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

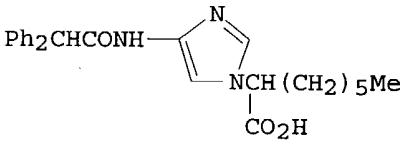
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2030961	AA	19910531	CA 1990-2030961	19901127 <--
US 5073566	A	19911217	US 1989-444456	19891130 <--
EP 438869	A1	19910731	EP 1990-312913	19901128 <--
EP 438869	B1	19941214		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ES 2064665	T3	19950201	ES 1990-312913	19901128 <--
JP 03193745	A2	19910823	JP 1990-336864	19901129 <--
JP 2935740	B2	19990816		
US 5312936	A	19940517	US 1991-761127	19910917 <--
US 5571925	A	19961105	US 1994-183685	19940119 <--
US 5563278	A	19961008	US 1995-453537	19950530 <--

PRIORITY APPLN. INFO.: US 1989-444456 19891130
US 1989-444465 19891130
US 1991-761127 19910917
US 1994-183685 19940119

OTHER SOURCE(S): MARPAT 115:256180
GI

Q=  Q1=  Q2= 

Q3=  Q4= 

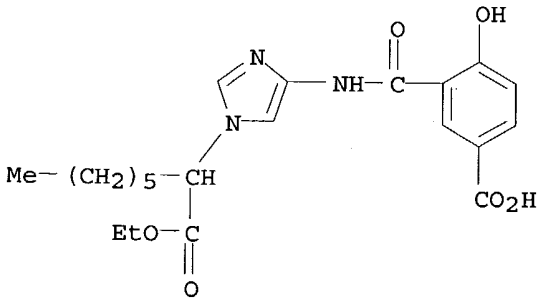


II

AB ArZGCHR1R2 [I; G = phenylene, bivalent 5-membered heterocyclic ring Q; Ar = substituted Ph, aromatic residue Q1-Q4; R1 = (CH2)nR3; R2 = C4-7 alkyl; Z = CO, CONH, NHCO, CH2CONH, O, NH, CH2, bond; R3 = HO, HO2C, 5-tetrazolyl; R4 = H, HO, halo, NO2, amino, Me, AcNH, MeSO2NH; A1-A3 = N, CH; W = Me, Et, HO; X = bond, O; n = 0-4] or their pharmaceutically acceptable salts or solvates, useful for **treating** congestive **heart failure** and angiotensin-induced hypertension, were prepared A solution of 41.8 g 4-nitroimidazole in DMF was refluxed 1 h with a suspension of NaH in DMF, the mixture was **treated** by 92 g Me(CH2)5CHBrCO2Et in DMF, and the whole refluxed for 2 h to give 10.40 g Et 4-nitro-α-hexyl-1H-imidazole-1-acetate. Hydrogenation of the latter (5.9 g) over Pd/C in EtOH gave 5.3 g 4-amino analog which (750 mg) was coupled with Ph2CHCO2H in the presence of carbonyldiimidazole in DMF to give 250 mg title compound (II·HCl). The latter at 10-5 M (test form unspecified) gave 80% inhibition of binding of 125I-angiotensin II to rat adrenal membranes. Formulations containing I are given.

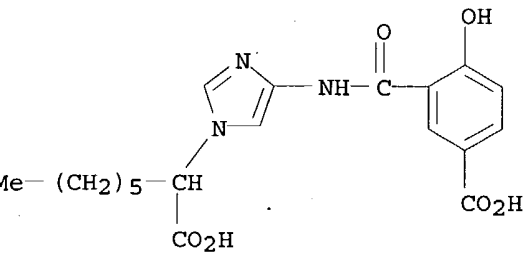
IT **137417-53-9P 137417-72-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as angiotensin II antagonist)

RN 137417-53-9 CAPLUS
CN 1H-Imidazole-1-acetic acid, 4-[(5-carboxy-2-hydroxybenzoyl)amino]-α-hexyl-, α-ethyl ester (9CI) (CA INDEX NAME)



RN 137417-72-2 CAPLUS
CN 1H-Imidazole-1-acetic acid, 4-[(5-carboxy-2-hydroxybenzoyl)amino]-α-

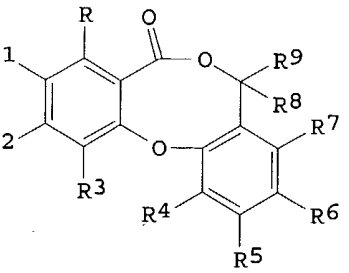
hexyl- (9CI) (CA INDEX NAME)



L6 ANSWER 23 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1991:428987 CAPLUS
DOCUMENT NUMBER: 115:28987
TITLE: Cardioactive dibenzo[1,5]dioxocin-5-one derivatives
INVENTOR(S): Frobel, Klaus; Lenfers, Jan Bernd; Fey, Peter; Knorr, Andreas; Stasch, Johannes Peter; Mueller, Hartwig; Bischoff, Erwin; Dellweg, Hans Georg
PATENT ASSIGNEE(S): Bayer A.-G., Germany
SOURCE: Ger. Offen., 60 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3919255	A1	19901220	DE 1989-3919255	19890613 <--
US 5089487	A	19920218	US 1990-528667	19900524 <--
AU 9056008	A1	19901220	AU 1990-56008	19900528 <--
AU 632578	B2	19930107		
NO 9002400	A	19901214	NO 1990-2400	19900530 <--
NO 175745	B	19940822		
NO 175745	C	19941130		
EP 411268	A2	19910206	EP 1990-110336	19900531 <--
EP 411268	A3	19910703		
EP 411268	B1	19950419		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 121396	E	19950515	AT 1990-110336	19900531 <--
ES 2072332	T3	19950716	ES 1990-110336	19900531 <--
CA 2018659	AA	19901213	CA 1990-2018659	19900611 <--
DD 298423	A5	19920220	DD 1990-341537	19900611 <--
HU 54136	A2	19910128	HU 1990-3811	19900612 <--
JP 03024073	A2	19910201	JP 1990-151794	19900612 <--
ZA 9004524	A	19910424	ZA 1990-4524	19900612 <--
CN 1048041	A	19901226	CN 1990-104489	19900613 <--

PRIORITY APPLN. INFO.: DE 1989-3919255 19890613
OTHER SOURCE(S): MARPAT 115:28987
I



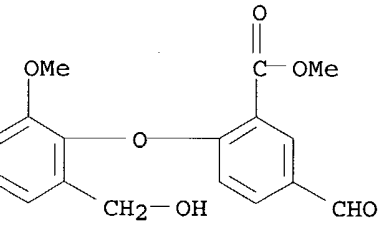
I

AB Penicillide derivs. I (R-R7 = H, (un)substituted alkyl, alkenyl, alkynyl; R8, R9 = H, (un)substituted alkyl] were prepared for use as antihypertensives, antiarrhythmics, and in the **treatment** of cardiac insufficiency (no data). Thus, I (R = R2 = R3 = R5-R9 = H, R1 = CHO, R4 = OMe) was obtained by alkoxylating 2,5-Br[(MeO)2CH]C6H3CO2Me with 2-methoxy-6-(2-tetrahydropyranyloxymethyl)phenol, ether cleavage, hydrolysis, and lactonization. Many I were prepared from penicillide.

IT **134563-73-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and ester hydrolysis of)

RN 134563-73-8 CAPLUS

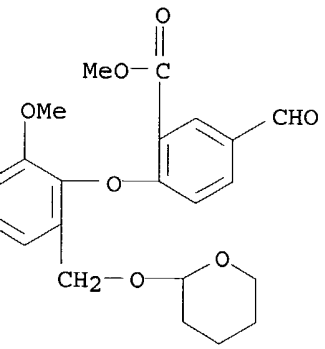
CN Benzoic acid, 5-formyl-2-[2-(hydroxymethyl)-6-methoxyphenoxy]-, methyl ester (9CI) (CA INDEX NAME)



IT **134563-70-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and ether cleavage of)

RN 134563-70-5 CAPLUS

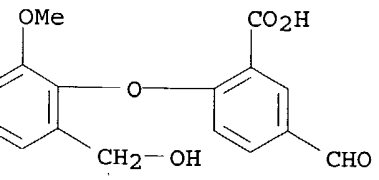
CN Benzoic acid, 5-formyl-2-[2-methoxy-6-[[(tetrahydro-2H-pyran-2-yl)oxy]methyl]phenoxy]-, methyl ester (9CI) (CA INDEX NAME)



T **134563-81-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and lactonization of)

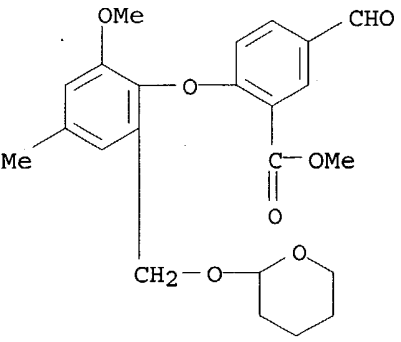
N 134563-81-8 CAPLUS

N Benzoic acid, 5-formyl-2-[2-(hydroxymethyl)-6-methoxyphenoxy]- (9CI) (CA INDEX NAME)



T **134563-71-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of)
RN 134563-71-6 CAPLUS
CN Benzoic acid, 5-formyl-2-[2-methoxy-4-methyl-6-[[(tetrahydro-2H-pyran-2-yl)oxy]methyl]phenoxy]-, methyl ester (9CI) (CA INDEX NAME)



L6 ANSWER 24 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1991:228897 CAPLUS
DOCUMENT NUMBER: 114:228897
TITLE: Preparation of saccharin derivatives useful as proteolytic enzyme inhibitors.
INVENTOR(S): Dunlap, Richard Paul; Boaz, Neil Warren; Mura, Albert Joseph; Hlasta, Dennis John
PATENT ASSIGNEE(S): Sterling Drug Inc., USA
SOURCE: PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

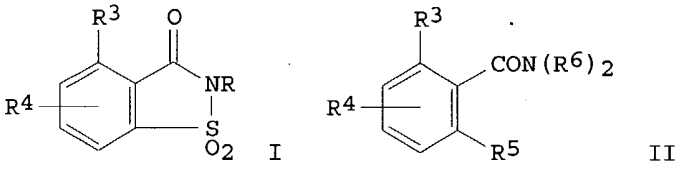
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9013549	A1	19901115	WO 1990-US2434	19900501 <--
W: AU, FI, JP, KR, NO				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
CA 1336960	A1	19950912	CA 1989-611223	19890913 <--
CA 1340252	A1	19981215	CA 1989-611220	19890913 <--
AU 9056649	A1	19901129	AU 1990-56649	19900501 <--
AU 637614	B2	19930603		
EP 471756	A1	19920226	EP 1990-907695	19900501 <--
EP 471756	B1	19971029		
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
JP 04507095	T2	19921210	JP 1990-507810	19900501 <--
AT 159720	E	19971115	AT 1990-907695	19900501 <--
ES 2110414	T3	19980216	ES 1990-907695	19900501 <--
IL 94278	A1	19950330	IL 1990-94278	19900603 <--
DD 297644	A5	19920116	DD 1990-343934	19900910 <--
NO 9104217	A	19911028	NO 1991-4217	19911028 <--
US 5371074	A	19941206	US 1993-67637	19930524 <--
US 5380737	A	19950110	US 1993-113508	19930827 <--
US 5650422	A	19970722	US 1994-270964	19940705 <--
US 5464852	A	19951107	US 1994-289113	19940811 <--
FI 9404967	A	19941021	FI 1994-4967	19941021 <--
US 5578623	A	19961126	US 1995-445240	19950519 <--
US 5596012	A	19970121	US 1995-449152	19950524 <--
FI 9600488	A	19960202	FI 1996-488	19960202 <--
FI 9600489	A	19960202	FI 1996-489	19960202 <--
US 5773456	A	19980630	US 1996-719216	19960925 <--
US 5874432	A	19990223	US 1997-803297	19970220 <--

PRIORITY APPLN. INFO.:			
	US 1989-347125	A	19890504
	US 1989-347126	A	19890504
	US 1990-514920	B2	19900426
	WO 1990-US2434	A	19900501

US 1990-608068	B2	19901101
US 1991-782016	A	19911024
FI 1991-5093	A	19911029
US 1991-793033	A3	19911115
US 1991-793035	B1	19911115
US 1993-67637	A3	19930524
US 1993-113508	A3	19930827
US 1994-270964	B3	19940705
US 1994-289113	A3	19940811
FI 1994-4967	A	19941021
US 1995-445240	A3	19950519

OTHER SOURCE(S): MARPAT 114:228897

GI



I II

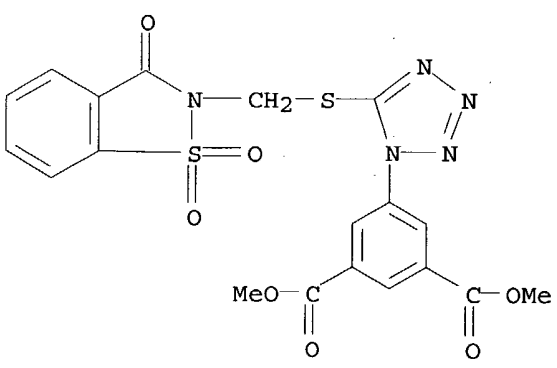
AB Saccharin derivs. [I; R = (CH:CH)mCHR2LnR1; L = O, S, SO, SO2; m, n = 0, 1; R1 = halo, alkanoyl, 1-oxophenalenyl, (substituted) Ph or heterocyclyl; R2 = H, carboalkoxy, Ph, PhS; R3 = H, halo, primary or secondary alkyl, alkoxy, carboalkoxy, Ph, fluoroalkyl, alkenyl, cyano; R4 = H, or 1 or 2 substituents selected from halo, cyano, NO2, (substituted) NH2, SO2NH2, OH, CHO, CH2OH, (polyhalo)alkyl, alkylsulfonyl, cycloalkyl, etc.], protease inhibitors useful in the **treatment** of, e.g., emphysema, **rheumatoid arthritis**, and pancreatitis, are prepared by, e.g., (1) reaction of I (R = CH2X; X = halo) with a LnR1 alkali metal salt; (2) reaction of I (R = H) with X1CHR2LnR1(X1 = halo); and (3) oxidation of I [R = CH(SPh)CH2CH2LnR1] to the sulfoxide followed by elimination to give I (m = 1, R2 = H). I (R = H) are prepared by lithiation of benzamides II (R3 = R5 = H, R6 = alkyl) followed by **treatment** with R3X2 (X2 = halo), lithiation of the resulting II (R3 = primary or secondary alkyl; R4,R6 = same as above) followed by reaction with SO2 and then a H2NOSO3H alkali metal salt, and heating the resulting I (R3, R6 = same above, R5 = SO2NH2) for cyclization. Thus, diazotization of Me 6-methylanthranilate with NaNO2 in concentrated HCl and AcOH followed by reaction with CuCl2.2H2O and SO3 gave Me 6-methyl-2-(chlorosulfonyl)anthranilate which was stirred with aqueous NH4OH to give 12% 4-methylsaccharin. Hydroxymethylation of the latter with HCHO in EtOH followed by acetylation with Ac2O in the presence of concentrated H2SO4 gave 73% I (R = CH2OAc, R3 = Me, R4 = H). A total of 124 I were prepared which in vitro inhibited elastase with Ki ≥ 0.3 nM.

IT **133743-27-8P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as protease inhibitor)

RN 133743-27-8 CAPLUS

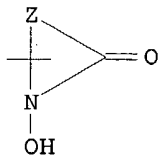
CN 1,3-Benzenedicarboxylic acid, 5-[5-[[(1,1-dioxido-3-oxo-1,2-benzisothiazol-2(3H)-yl)methyl]thio]-1H-tetrazol-1-yl]-, dimethyl ester (9CI) (CA INDEX NAME)



L6 ANSWER 25 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1990:515323 CAPLUS
DOCUMENT NUMBER: 113:115323
TITLE: Preparation of nonsteroidal antiinflammatory drugs
INVENTOR(S): Jackson, William Paul; Pettipher, Eric Roy
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9001929	A1	19900308	WO 1989-GB992	19890825 <--
W: JP, US				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
PRIORITY APPLN. INFO.:			GB 1988-20185	19880825
OTHER SOURCE(S):	MARPAT 113:115323			

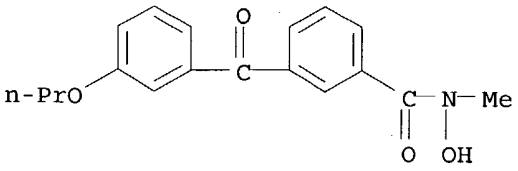
GI

Q1= 

AB Ar(LAr1)q(X)k(Y)pQ [I; k, p, q = 0.1; provided that when k = 1, p = 1; Ar = (un)substituted furyl, thienyl 1,1-dioxide, pyrryl, pyridyl, benzofuryl, Ph, etc.: L = (CH2)r, O, CH2O, CH2S, OCH2, CONH, NHCO, CO, CH2NH; r = 1-4; Ar1 = (un)substituted phenylene, thienylene, or pyridylene; X = O, S, CO; Y = C1-10 alkylene or alkenylene; Q = Q1, (CO)nN(OR1)(CO)mR2; m, n = 0, 1; when n = 1, m = 0 and R1,R2 = H, C1-4 alkyl or R2 = C5-7 cycloalkyl; when n = 0, m = 1, R1 = H, C1-4 alkyl, any one of Ar, alkanoyl, or (un)substituted CONH2 and R2 = H, C1-4 alkyl, NH2, C1-4 mono- or dialkylamino, anilino, etc.; Z = C2-5 alkylene optionally interrupted by a hetero atom], useful for **treatment** of arthritis, e.g., **rheumatoid arthritis**, rheumatoid spondylitis, **osteoarthritis**, gouty arthritis, or reactive arthritis, are prepared Thus, a solution of HSCH2CO2Me in THF was added dropwise to 1-(1-naphthyl)-2-nitroethene and Et3N in THF and after stirring 30 min at room temperature, the mixture was evaporated in vacuo, dissolved in saturated aqueous NH4Cl in 95 % EtOH, and then stirred 30 min with Zn powder to give 5,6-dihydro-1-hydroxy-5-(1-naphthyl)-1,4-thiazine-3(2H,4H)-one. A total of 88 I were prepared N-(3-Phenoxycinnamyl)acetohydroxamic acid (II) reduced the ovalbumin-induced swelling (arthritis) in the right knee joint of rabbits immunized with ovalbumin in Freund's complete adjuvant and II in combination with indomethacin, up to 51 %. Tablets and an injection solution containing II were formulated.

IT **106328-20-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as antiarthritic)

RN 106328-20-5 CAPLUS
CN Benzamide, N-hydroxy-N-methyl-3-(3-propoxybenzoyl)- (9CI) (CA INDEX NAME)



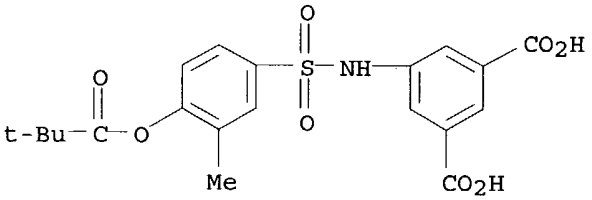
L6 ANSWER 26 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1990:514810 CAPLUS
DOCUMENT NUMBER: 113:114810
TITLE: Preparation of p-substituted phenyl ester of pivalic acid as elastase inhibitors and pharmaceutical compositions
INVENTOR(S): Imaki, Katsuhiro; Arai, Yoshinobu; Okegawa, Tadao
PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 91 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 347168	A1	19891220	EP 1989-305959	19890613 <--
EP 347168	B1	19930901		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 5017610	A	19910521	US 1989-364994	19890612 <--
CA 1340191	A1	19981215	CA 1989-602530	19890612 <--
JP 03020253	A2	19910129	JP 1989-148479	19890613 <--
JP 05081586	B4	19931115		
AT 93843	E	19930915	AT 1989-305959	19890613 <--
ES 2059752	T3	19941116	ES 1989-305959	19890613 <--
JP 06179645	A2	19940628	JP 1992-241380	19920819 <--
JP 06094450	B4	19941124		
US 5336681	A	19940809	US 1992-960301	19921013 <--
US 5403850	A	19950404	US 1994-235856	19940429 <--

PRIORITY APPLN. INFO.:

JP 1988-145450	19880613
JP 1989-53541	19890306
US 1989-364994	19890612
EP 1989-305959	19890613
US 1991-681364	19910408
US 1992-960301	19921013

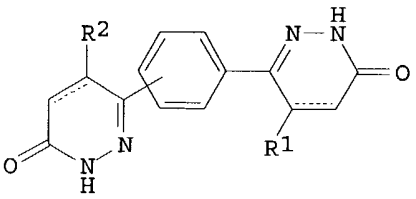
OTHER SOURCE(S): MARPAT 113:114810
GI For diagram(s), see printed CA Issue.
AB The title esters [I; Y = SO2, CO; R1,R2 = H, (substituted) C1-16 alkyl, Q (wherein X = bond, SO2, C1-4 alkylene optionally substituted with CO2H or CO2CH2Ph; ring A is carbocyclic or heterocyclic; R4 = H, C1-8 alkyl, C1-4 alkoxy, etc.; n = 1-5), R1R2N = (substituted) heterocyclic; R3 = H, OH, C1-6 alkyl, halo, C1-4 alkoxy, C2-5 acyloxy, m = 1-4], useful as elastase inhibitors in **treating** or preventing pulmonary emphysema, atherosclerosis, and **rheumatoid arthritis**, are prepared Pivaloyl chloride (0.5 mL) was added to a solution of II (R = H) (preparation given) in Et3N-CH2Cl2 under cooling and the solution was stirred 1 h at room temperature to give 510 mg II (R = pivaloyl), which showed elastase inhibition at 0.031 μM. Also prepared were 134 addnl. I.
IT **127373-55-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as elastase inhibitor)
RN 127373-55-1 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-[[[4-(2,2-dimethyl-1-oxopropoxy)-3-methylphenyl]sulfonyl]amino]- (9CI) (CA INDEX NAME)



L6 ANSWER 27 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1987:156489 CAPLUS
DOCUMENT NUMBER: 106:156489
TITLE: Bis(6-oxopyridazinyl)benzene derivatives as drugs
INVENTOR(S): Prain, Hunter Douglas; Warrington, Brian Herbert
PATENT ASSIGNEE(S): Smith Kline and French Laboratories Ltd., UK
SOURCE: Eur. Pat. Appl., 28 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 208517	A2	19870114	EP 1986-305187	19860704 <--
EP 208517	A3	19880323		
EP 208517	B1	19900912		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
IL 79280	A1	19900712	IL 1986-79280	19860630 <--
US 4904664	A	19900227	US 1986-880849	19860701 <--
AU 8659488	A1	19870108	AU 1986-59488	19860702 <--
AU 580677	B2	19890127		
DK 8603169	A	19870106	DK 1986-3169	19860703 <--
ZA 8604954	A	19870225	ZA 1986-4954	19860703 <--
FI 8602840	A	19870106	FI 1986-2840	19860704 <--
NO 8602723	A	19870106	NO 1986-2723	19860704 <--
JP 62012765	A2	19870121	JP 1986-158634	19860704 <--
JP 05086951	B4	19931214		
HU 41393	A2	19870428	HU 1986-2821	19860704 <--
ES 2000209	A6	19880116	ES 1986-129	19860704 <--
AT 56440	E	19900915	AT 1986-305187	19860704 <--
CN 86105663	A	19870121	CN 1986-105663	19860705 <--
PRIORITY APPLN. INFO.:			GB 1985-17051	19850705
			GB 1986-6853	19860320
			EP 1986-305187	19860704

GI



I

AB The title compds. (I; R1, R2 = H, Me; dotted lines = optional double bonds; the benzene ring is m- or p-substituted) were prepared as phosphodiesterase inhibitors, useful in **treating** congestive **heart failure**. C6H4(COMe)2-1,4 condensed with HCOCO2H to give 1,4-(HO2CCH:CHCO)2C6H4 which cyclocondensed with N2H4 to give I (R1 = R2 = H, dotted line = bond, p-substituted) (II). In cats 0.04 μmol II/kg increased left ventricular contractility 50%. Capsules were prepared containing active ingredient 0.5, soya lecithin/soybean oil 90.45, hydrogenated vegetable oil/beeswax 9.05%.

IT **107549-79-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclocondensation of, with piperazine)

RN 107549-79-1 CAPLUS
CN 2-Butenoic acid, 4,4'-(1,3-phenylene)bis[4-oxo- (9CI) (CA INDEX NAME)